A

PRACTICAL TREATISE

ON

RENAL DISEASES

AND

URINARY ANALYSIS

BY

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CONTAINING ONE HUNDRED ILLUSTRATIONS

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THE FOLLOWING PAGES

ARE DEDICATED TO

MY FATHER,

FREDERICK EDWARD PORTER,

AS A TOKEN OF RESPECT

AND AFFECTION.

PREFACE.

DURING the past ten years, the author has had ample opportunity for studying the various lesions of the kidneys, as they are found in human and animal subjects. The essential ideas advanced in this book, if any originality can be claimed, are based upon the statistics gathered from over one thousand post-mortems.

Attention was devoted specially, during the course of studies in comparative medicine, to the class of lesions commonly known as Bright's disease, and it was from these observations, taken in connection with the opportunities that have offered since of watching these conditions from their inception in the human being, through the different phases of the disease, until finally they came to the post-mortem table, that the deductions employed throughout the work were obtained.

Among the lower animals, the necropsies were made immediately after death, and consequently accurate results were obtained in regard to the morbid changes in the epithelial protoplasm, and the examiner was enabled to judge how much of the metamorphotic change was due to the disturbed physiological condition prior to death, and how much was more directly due to the post-mortem alterations.

Renal diseases have been studied chiefly from the clinical and pathological point of view, but we have tried to present them not only from this standard, but also from the physiological standpoint, deducing the methods of treatment not only from the physiological, but from the pathological phenomena.

Preceding the group of diseases usually classed as Bright's disease, a brief resumé of the anatomy and physiology of the kidneys has been inserted, in order that the reader, by refreshing his memory, may be

enabled to obtain a clear understanding of the various lesions; and in connection with this, the various pathological conditions found are described at some length.

A chapter is also devoted to the consideration of diabetes.

The second portion of the book is devoted to a study of urinary analysis; not simply the chemical or microscopical examination of samples of urine, but also the physiological indications, with their bearings on clinical medicine. A more accurate interpretation of the exact conditions of the diseased organs may be obtained, and a more definite prognosis pronounced, when these considerations receive full weight, than can be the case if only the chemical and microscopical results, as usually noted, are borne in mind.

An extended bibliography has been omitted purposely, in order that the work might be kept within bounds; but the author takes this opportunity of acknowledging the assistance obtained by a perusal of the chief authorities upon both renal diseases and urinary analysis.

The original drawings, some fifty in number, have been made by his clinical assistant, Dr. George G. Van Schaick, from sections in the author's possession, and the credit is due him for their accuracy and perfection.

Through the courtesy of Dr. Francis Delafield and the kind co-operation of the publishers, Messrs. William Wood & Co., a large number of plates have been employed in illustrating different portions of the book, that have appeared in other works on this subject.

It gives me much pleasure, also, to testify to the valuable aid I have received from two of my former students, Dr. William C. Carroll and the late Dr. William Hustace Hubbard.

Before closing, the author wishes to extend his sincere thanks to his friend, Dr. Samuel Lloyd, who has rendered most valuable aid in the final revision of the manuscript and in the correction of the proofs.

<div style="text-align: right">W. H. P.</div>

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RENAL DISEASES.

PART I.

CHAPTER I.

ANATOMY OF THE KIDNEY.

The kidneys, the two largest glandular organs in the body, are intended for the excretion of urine, and are situated in the lumbar region, on either side of the vertebral column; the left on a level with the last dorsal and two upper lumbar vertebræ, the right lying somewhat lower, on account of the large space occupied by the liver. They rest upon the crura of the diaphragm, behind the peritoneum, the upper end approaching nearer the vertebral column than the lower; and they have a quantity of connective tissue and fat called the *tunica adiposa* surrounding them, which, together with their blood-vessels, nerves, lymphatics, and ureters, holds them in proper position, and through which they receive their nutriment and discharge their excretions. They are about four inches (10 centimetres) in length and one inch (2.5 centimetres) in thickness, but these dimension vary in individual cases. The left is usually larger and narrower than the right, and weighs one and a half drachms more. The average weight of the kidney in the adult male is from four and a half to five ounces (125.572–141.747 grams); and in the adult female from four to four and a half ounces (113.398–127.572 grams). The specific gravity of the kidney tissue is about 1.052.

Regional Relations and Topography.—The anterior surface of the left kidney is in contact with the inferior extremity of the spleen and the tail of the pancreas; covered in by the cardiac extremity of the stomach, and is immediately behind the descending colon. The anterior surface of the right kidney is in contact with the liver and de-

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scending portion of the duodenum, and is immediately behind the ascending colon. Both are covered anteriorly by the peritoneum, the tunica adiposa intervening.

The posterior surface of each kidney rests against the corresponding crus of the diaphragm and the anterior lamella of the transversalis fascia which covers the quadratus lumborum muscle ; the superior extremity is in contact with the corresponding suprarenal capsule.

Variations.—From the normal standard above described, the kidneys occasionally vary as regards form, position, size, and number. Sometimes they are long and narrow, sometimes short and broad; one or both may be situated in the pelvic region or any other part of the abdominal cavity; the vessels may be elongated, the peritoneum forming as it were, a mesentery, and thus allowing them to float freely in the peritoneal cavity, giving rise to the condition known as a "floating kidney," which is most frequently met with in women, and usually on the right side.

One kidney may be large and the other proportionately small; or the two may be united by a band of renal tissue, passing over the vertebræ and connecting their inferior extremities; this condition is known as a "horse-shoe" kidney; and when it occurs, both glands are usually situated lower than normal.

One kidney and its ureter may be entirely absent, the opposite organ being normal or increased in size; and in rare instances three have been found in one body, the third occupying a position in front of the vertebral column, or at the side of the normally located glands. There is one case on record in which there were four with their accompanying vessels and ureters; [1] all four ureters opening separately into the bladder. The two kidneys have also been found upon the same side, and in such cases they are usually located lower than normal.

The surface may be traversed by numerous moderately deep furrows which give the organ a distinctly lobulated appearance; this condition is always present in the fœtal kidney, and may be found in organs removed from the bodies of those who die during the first few years of life; but this is not usually the case in those removed from adults, the external surface being then perfectly smooth. When traces of these furrows and lobules are found in the adult organ, they are called *traces of or fœtal markings*. This condition is not infrequently met with, and indicates only a divergence from the general rule, having no pathological significance.

Macroscopic Appearance.—The kidney is shaped somewhat like a

[1] Indiana Medical Gazette, Jan., 1874.

" Haricot " or " Kidneybean." The anterior surface is convex, the posterior nearly flat; the superior extremity is thick and rounded, and is larger than the inferior, which is thinner and more pointed. The external border is convex, the internal concave, presenting a deep fissure, about an inch (2.5 centimetres) in length, called the *hilum*, through which pass the vessels, nerves, and lymphatics, and the excretory duct or ureter. The hilum opens into a cavity in the substance of the gland which is called the *sinus renalis*.

The relations of the vessels and ureter to each other in the hilum are as follows: from above downwards, artery, vein, and ureter; from
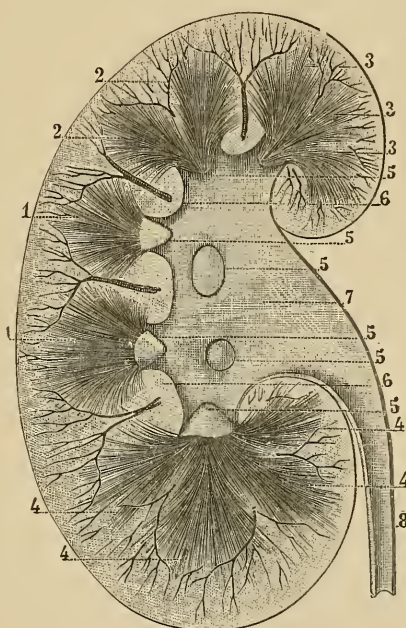
FIG. 1.—CROSS SECTION OF KIDNEY.

1, Malpighian pyramid; 2, arterio-venous arcade of Flint; 3, striations of the pyramid; 4, base of pyramids of Ferrein; 5, calices; 6, columns of Bertini; 7, pelvis and infundibuli; 8 ureter. (From Sappey's Anatomy.)

before backward, vein, artery, and ureter; but this arrangement occasionally varies. The whole gland is covered by a thin, smooth, fibrillated connective-tissue membrane, called the capsule, which, in the normal state, is not adherent to the underlying surface, and, upon removal, leaves it perfectly smooth, although the fœtal markings may occasionally be observed. By making a longitudinal section, the cortex, medullary substance, and sinus renalis are exposed. *The sinus*

renalis is the deep fossa in the kidney proper in which the pelvis (the expanded portion of the ureter) joins the renal substance, and through which the vessels pass to reach the nephritic tissue. The *hilum* is the perceptible notch; the *sinus* is deep in the gland proper. The medullary substance consists of from eight to eighteen conical masses called the *Pyramids of Malphigi;* their apices being known as *papillæ,* which converge and are invaginated in the ultimate divisions of the pelvis known as the *calices.* The calices, seven to thirteen in number, converge to form the three primary divisions of the pelvis, which in turn have been termed *infundibula;* and these join to form the *pelvis* of the kidney, which is the funnel-shaped extremity of the dilated ureter. The ureter is the excretory duct, and opens into the posterior surface of the bladder. The pyramids are distinctly striated, these
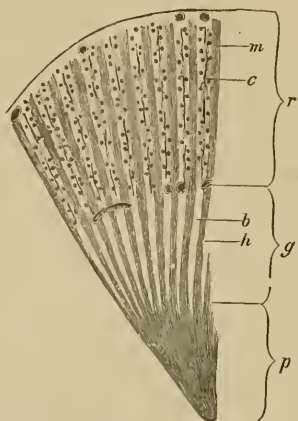
FIG. 2.—MARKINGS OF THE CORTEX.

r, Cortical layer; *m,* medullary rays or pyramids of Ferrein; *c,* arteriæ rectæ, with attached Malpighian corpuscles; *g,* base of Malpigian pyramid; *h,* bundle of collecting tubes; *b,* vascular area between the bundles; *p,* apex of Malpighian pyramid.

striations always being straight in the normal kidney, and consisting of diverging blood-vessels and straight or collecting uriniferous tubules, the arrangement of which will be explained hereafter. This striated appearance is prolonged into the cortex, where it is more prominent than in the pyramids. This is accounted for by the greater paleness of the epithelium. The red lines indicate the position of the nutrient vessels; the pale lines indicate the straight tubules prolonged into the cortex, and are known as the *Pyramids of Ferrein.* These alternating colors are called the *markings* of the *cortex;* when straight, they indicate a normal kidney, or one in which the lesion is confined to the epithelial cells only; when wavy or tortuous, they indicate a lesion in-

volving the intertubular tissue, which by contraction has caused the vessels to deviate from a straight course. By these striations and their changes, we are enabled, in a measure, to differentiate between a parenchymatous and a diffuse or sclerotic change. This will be fully appreciated later on, when studying the morbid appearances.

The cortical layer lies immediately beneath the renal capsule; it is about one-quarter of an inch (6.25 mm.) in thickness, and surmounts the base of the pyramids, sending prolongations between them as far as the sinus. These interpyramidal portions are known as the "*Septa vel Columnæ Bertini*," and mark the original divisions of the kidneys into lobules. That portion of the cortical substance which stretches from one column to another, and which surrounds the base of the pyramids, is called the *cortical arch*. The columns of Bertini and the cortical arches taken together form the "*Labyrinth of Ludwig.*"[1]

Microscopic Appearances.—The capsule is composed of fibrous tissue, in which a few elastic fibres are intermingled.

It is connected with the organ by fine fibrillated connective tissue and minute blood-vessels. An inflammatory thickening and an increase in these connecting fibres account for the adhesion of the capsule and the roughening and detachment of small fragments of the renal surface in the intertubular varieties of renal disease.

The capsule may be divided into two layers: an outer one about $\frac{1}{175}$ of an inch (0.143 mm.) in thickness, which becomes continuous with the connective tissue surrounding the blood-vessels and the ureter at the hilum; and an inner, about $\frac{1}{1000}$ of an inch (0.025 mm.) in thickness, terminating where the papillæ join the calices in the sinus renalis. Beneath the latter is a wide-meshed, delicate framework of smooth muscle fibres, some of which traverse the cortical substance.

The uriniferous tubules begin in the cortical substance in small spherical bodies called the *Malpighian corpuscles*, beyond which they are markedly convoluted, and are known as the *convoluted tubes of the first order*.

At the junction of the capsules with the tubes, there is a marked constriction or *neck*, and beyond this convoluted portion they become straight and pass directly down into or between the pyramids, forming the *descending limb*, then turning upon themselves they form a *loop* and pass straight upwards to the cortical arches or substance, thus forming the *ascending limb;* and these, taken together, form the *looped tube of Henle.* In the cortical substance, the tubules again be-

[1] Ludwig: Stricker's Manual, p. 461.

come convoluted and are called *junctional* tubes, *intercalated* tubes, or *convoluted tubes of the second order*. They now become straight and pass down through the pyramids toward the papillæ, being
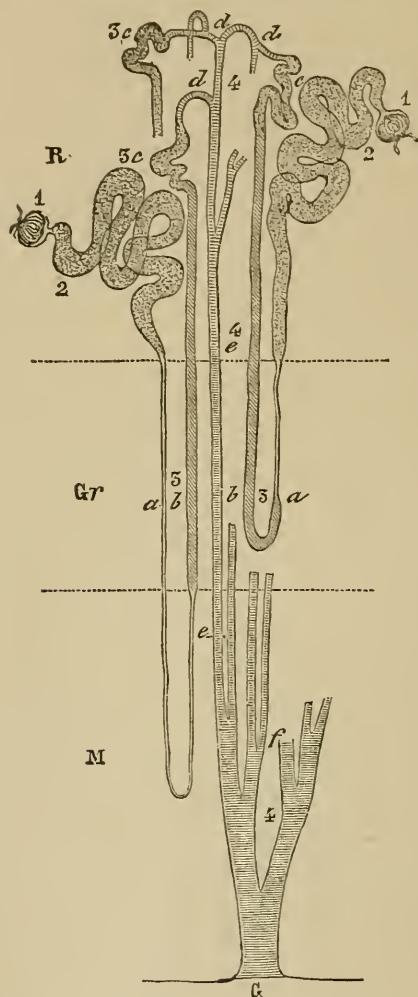
FIG. 3.—DIAGRAM OF URINIFEROUS TUBULES.

R, Cortical Portion. 1, Malpighian tuft; 2, convoluted tube of first order showing neck; 3 c, convoluted tube of second order; d, straight portion of tube between convoluted tube of second order and collecting tube; 4, collecting tube near surface of kidney; 4 e, collecting tube entering cortico-medullary portion. Gr, Cortico-Medullary Portion. 3, loop of Henle; (a), descending arm; (b), ascending arm. M, Medullary Portion. 4, converging collecting tube; e, collecting tubes; f, intertubular space; g, opening of uriniferous tubule at apex of Malpighian pyramid.

called the *straight* or *collecting* tubes, and, after uniting at very acute angles, form the excretory tubes or *ducts of Bertini*. These empty into the calices on the surface of the papillæ, sometimes at the bottom of a slight depression, known as the *foveola*, but more often their open mouths are dotted over the surface. The straight or collecting tubes, just before leaving the cortical substance, are arranged in bundles, the central tubes of which are the longest, while the most external are the shortest; this difference in length gives the bundles a pyramidal appearance, from which they have been called the *pyramidal prolongations, medullary rays, or pyramids of Ferrein*. They are found only in the cortical arches, and are also known as *lobules* of the kidney.
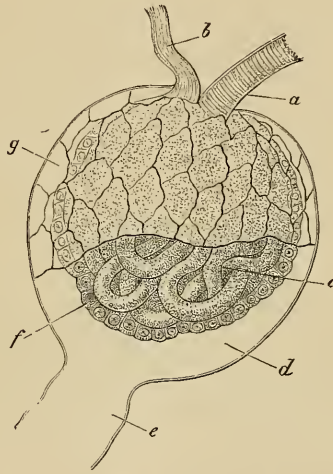
FIG. 4.—MALPIGHIAN TUFT (Highly Magnified).

a, Afferent artery; *b*, efferent vein: *c*, neck of uriniferous tubule; *d*, space within the capsule; *f*, capillary network; *g*, epithelial lining of Bowman's capsule.

The tubules consist throughout their whole extent of a basement-membrane lined with epithelium. The Malpighian corpuscles are small spherical bodies, regularly arranged in rows in the edges of the pyramids of Ferrein in the cortical arches, but they are also scattered irregularly throughout the columns of Bertini. They vary from $\frac{1}{100}$ to $\frac{1}{270}$ of an inch (0.25 mm.–0.092 mm.) in diameter, and are composed of an investing or external capsule known as *Bowman's, Müller's,* or the *Malpighian* capsule.

This capsule is composed of an investing basement-membrane lined with flat epithelial cells, reflected over the glomerulus, and often

dipping in between the individual blood-vessels. The glomerulus is
formed by a small afferent artery dividing into a number of convo-
luted loops, that unite to form an efferent vessel, which is
smaller than the afferent. The two vessels pierce the capsule at
points very near each other. Almost directly opposite their point of
entrance and exit, the capsule becomes continuous with the convo-
luted tube of the first order which has an average diameter of
$\frac{1}{600}$ of an inch (0.041 mm.). It is composed of a basement-
membrane lined with epithelial cells, which are somewhat triangular
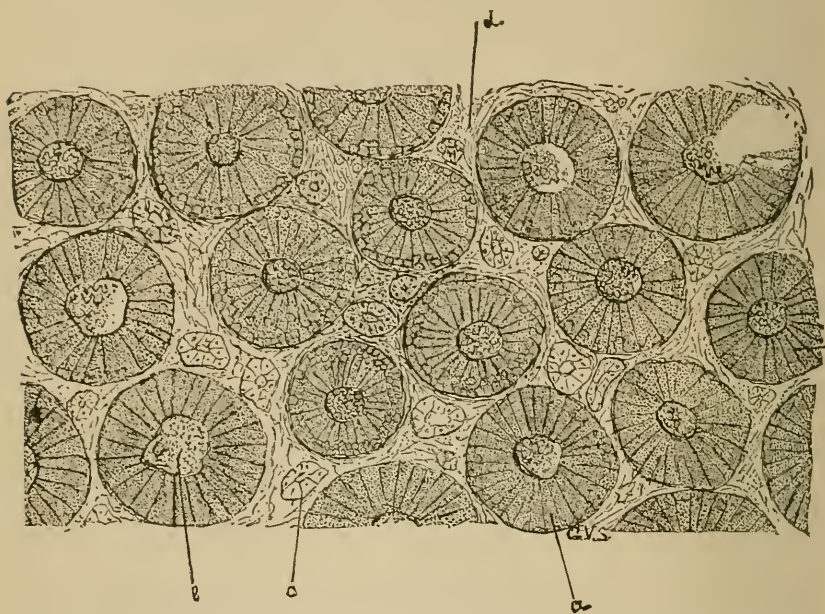
Fig. 5.—Section from Snake's Kidney Showing the Rods of Heidenhain.
a, Uriniferous tubules with rods; c, tubules without rods; d, intertubular tissue.

in character, and which project more than half-way across the
diameter of the tube. Owing, however, to the fact that the projection
on one side is between two projections on the opposite side, the lumen
is not closed, but has a spiral character. These epithelial cells have
a striated appearance, produced by capillary tubules, one end of
which rests against the basement-membrane, while the other projects
towards the lumen of the tube. These are called the " Rods of
Heidenhain." The looped tubules traverse the pyramids for a greater
or less distance, and some almost reach the papillæ, while others
scarcely enter the medullary substance. The average diameter of the

descending limb is $\frac{1}{1250}$ (0.020 mm.), diminishing in some places to $\frac{1}{2000}$ of an inch (0.012 mm.).

The diameter of the ascending limb is about $\frac{1}{600}$ of an inch (0.041 mm.); the lumen in the latter case, however, is the smaller of the two. The ascending limb is similar in construction to the convoluted tubules of the first order, but it is larger than the descending limb, and ends in the convoluted tube of the second order.

The epithelial cells lining the descending arm are spheroidal and sparsely set, and the nuclei being large, cause the cells to project into the lumen, giving it a tortuous appearance on longitudinal section.

The epithelial cells of the ascending limb are cuboidal; those of the intercalated portion are pyramidal, resembling those of the first order.

FIG. 6.—LOOPED TUBE OF HENLE.
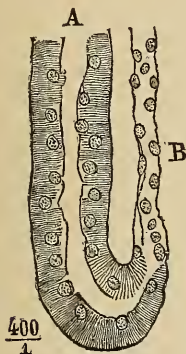
FIG. 7.—PRICKLE CELLS TAKEN FROM KIDNEY OF DOG.

B, Descending limb showing the spindle-shaped epithelial cells; *A*, ascending limb showing cuboidal epithelium with "Rods of Heidenhain."

a, From smallest collecting tubes: *b*, from larger collecting tubes. × 450 (Satterthwaite's Histology.)

In the convoluted portions of both the first and second orders, and in the ascending limb of Henle, the epithelial cells contain the "Rods of Heidenhain."

The collecting tubules gradually increase in size as they approach the papillæ. In the upper part of their course they are about $\frac{1}{600}$ of an inch (0.041 mm.) in diameter, but this increases near the papillæ to $\frac{1}{430}$ or $\frac{1}{240}$ of an inch (0.051–0.104 mm.). The epithelial cells lining this part of the tubules are of the columnar variety, the only peculiarity being that their bases are irregular in shape and in-

terdigitate, the projections of one fitting in the other. They are a form of prickle cell.

The kidney receives its *supply* of *blood* through the renal artery, which, passing through the hilum, between the ureter and vein, enters the sinus renalis and there divides into a number of branches, which spread among the infundibuli and enter the columns of Bertini. Here they subdivide and proceed in straight lines to the cortical substance, where they form arches around the base of the pyramids. These arches are not so complete as those formed by the accompanying veins. The two arches taken together are known as the arterio-venous *Arcade of Flint*. From the arches small branches are given off, called the *intertubular arteries,* which pass outward between the double rows of Malpighian corpuscles, intervening be-
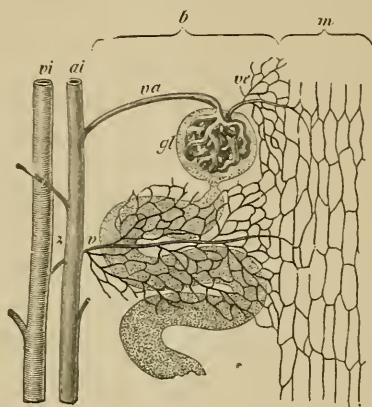
FIG. 8.—SECTION SHOWING VASCULAR ARRANGEMENT OF THE KIDNEY.

b, Zone of arteriæ rectæ and Malpighian corpuscles; *m*, zone containing the pyramids of Ferrein and the intertubular plexus; *vi*, venæ rectæ; *ai*, arteriæ rectæ; *va*, afferent artery; *gl*, glomerulus; *ve*, efferent vein; *v*, vein from intertubular plexus; *z*, entrance of vein into venæ rectæ.

tween the pyramids of Ferrein, to which they give off branches, viz., the afferent arteries of the Malpighian bodies. The renal arteries also give off branches to the capsule, which anastomose freely with branches from the lumbar arteries. From the lowermost of the Malpighian tufts, and also from branches of the renal artery, straight vessels pass downward toward the apex of each pyramid and break up into capillaries, which surround the collecting tubules; these are known as *arteriæ rectæ*. The blood in returning flows through a corresponding set of veins and finally empties into the intertubular veins. From the Malpighian corpuscle the efferent vessel divides into a net-

work of capillaries, which surround the tubules of the cortical substance and form the *intertubular plexuses,* which, as they approach the cortex, form small veins. The small radicles anastomose with one another near the surface of the gland, and from their peculiar star-shaped arrangement are called *the stellated veins or " Stars of Verheyen."*

This stellated appearance is more a pathological than a histological condition, for it is not always present; and when it is distinct, the vessels of the kidneys are usually in a state of dilatation, which has resulted from obstructive congestion. They, however, have been commonly described under the normal histological appearances. These stellar veins are the primary origin of the *intertubular* or *interlobular veins,* which pass downward and accompany the intertubular arteries to the venous side of the arterio-venous arcade. From the arcade the venous trunks proceed in company with the arteries in the pyramids of Bertini to the sinus of the kidney, where they ultimately join to form the renal vein.

The *nerves* that have been traced into the kidney are small and derived from the solar plexus; some coming directly from the renal plexus, and some from the smaller splanchnic nerve. There are also some filaments derived from the cerebro-spinal system. They follow the course of the arteries and have been traced for some distance, but their manner of termination is uncertain.

The *lymphatics* are numerous, and arranged in two sets; one a superficial plexus in the fibrous capsule, the other a deep or internal plexus which emerges from the sinus in company with the blood-vessels. The internal form a freely communicating plexus of lymph spaces, most marked around the tubules of the cortex. This central plexus communicates with the lymphatics of the capsule and those issuing from the sinus.

The *stroma* of the kidney is made up of a variety of connective-tissue elements. The fibres are most numerous in the vicinity of the blood-vessels and around the Malpighian corpuscles; they are more marked in the cortical than in the medullary portion, but become abundant near the apices of the papillæ. The stroma is abundant in the kidneys of infants, but is difficult to demonstrate in the adult organ. This latter fact has led some to deny the existence of any stroma whatever. This, however, is not generally recognized to be true, and most, if not all histologists, believe in its presence.

CHAPTER II.

PHYSIOLOGY OF THE KIDNEY; INFLAMMATION AND ITS BEARINGS ON THE PATHOLOGY AND TREATMENT OF ACUTE PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEY.

During the past few years, many advances have been made, by carefully conducted physiological experiments, in our knowledge of the excretory function of the kidney and its histological and pathological anatomy, so that we are now in a position to understand better than ever many of the topics of Bright's disease (so-called) that have been unsatisfactory and obscure.

If, then, we keep these newly acquired physiological data in mind, and study the pathological changes, it will be easy to see that the common term, Bright's disease, covers a number of renal lesions. These naturally fall into groups that are quite distinctive, and, in nearly every instance, have such peculiar clinical characteristics that they can be recognized nearly as well at the bedside as on the post-mortem table.

In the present chapter it is proposed to take up one form of a single group, in which the morbid changes affect the epithelial elements, and it may be here stated that the data employed were obtained by a study of cases which were followed from the ward to the post-mortem table. It is hoped that the views here advanced will contribute, not only to our knowledge of the disease from the purely pathological standpoint, but will serve to show the relation of the changes to the general condition of the patient, so that our treatment in such cases may be better directed.

It must be recognized that there are two subdivisions of the excretory apparatus of the kidney—one composed mainly of the coil of blood-vessels in the glomerulus, or Malpighian tuft, the other of the epithelium lining a portion of the tubules.

The glomeruli are generally believed to filter the water and inorganic salts held in solution; it is also thought that sugar, albumin, and peptones pass out through the glomeruli, the epithelium of the

tubules eliminating the urea and the crystalline nitrogenous sub-
stances.

Now, as the passage of solutions through an animal membrane
depends to a great extent upon the pressure exerted, the rapidity
with which the urine is excreted and its amount naturally vary with
the blood-pressure in the glomeruli, and, consequently, the greater
the pressure in the vessels the greater will be the excretion, and
vice versa. Accordingly, the pressure in the vessels of the glomeruli
may be increased—

1. By any increase in the force and frequency of the heart's action.

2. By contraction of the arterioles at large or in areas other than
those of the kidney.

3. By relaxation of the renal arterioles, either alone or with con-
traction of other areas.

Or the pressure may be diminished—

1. By any diminution in the force and frequency of the heart
beats.

2. By dilating the arterioles at large or in areas other than the
kidney.

3. By contraction of the renal arterioles, either alone or with relaxa-
ation of other areas.

The function of the glomeruli is comparatively simple, being
immediately under the control of the vaso-motor system. Physio-
logical experiments have shown that a division of the spinal cord
below the medulla greatly diminishes the flow of urine. The expla-
nation is, that large vascular areas are cut off from their communica-
tion with the medullary vaso-motor centre, which, associated with the
shock to the spinal cord, produces a great fall in the general blood-
pressure.

With this relaxation of the renal artery an augmented flow of urine
would be expected, but the great fall in the general blood-pressure com-
pletely overbalances the effect produced upon the renal artery and di-
minishes the pressure in the vessels of the glomeruli. Stimulating the
spinal cord below the medulla affects the cord in an opposite manner
from division, but produces the same effect in reference to the quantity
of urine excreted. This is explained by the renal artery becoming so
firmly contracted that the general increased blood-pressure is over-
balanced, the artery being, as it were, ligated, and the pressure upon
the vessels of the glomeruli diminished or removed. Therefore,
opposite effects upon the cord produce precisely the same action upon
the glomeruli.

Section of the renal nerve produces relaxation of the renal artery,

increased pressure in the capillaries of the glomeruli, and an increased flow of urine. Section of the spinal cord, after division of the renal nerve, arrests the polyuria by increasing the general capillary capacity outside the kidney, thus reducing the general blood-pressure, and in this way again establishing a normal pressure in the glomeruli. Stimulation of the spinal cord, after division of the renal nerve, still further increases the flow of urine by diminishing the general capillary capacity outside the kidney, thus increasing the general blood-pressure in the glomeruli.
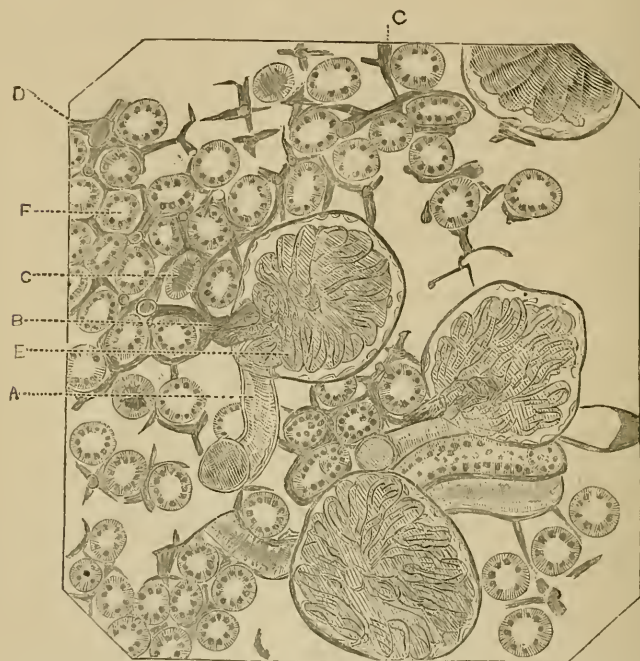
FIG. 9.—KIDNEY OF DOG. NATURAL INJECTION OF SECRETING PORTION, ARTIFICIAL INJECTION OF ARTERY, VEIN, AND CAPILLARIES. TRANSVERSE SECTION THROUGH CORTICAL SUBSTANCE.

a, Afferent vessel, filled with injected material; b, efferent vessel, also filled with injection; e, glomerulus, injected and lying within its capsule, epithelium of latter distinctly seen; d, capillaries surrounding the convoluted tubules, and distended with the injection, at this point four capillaries are seen to unite and form a vein; c, convoluted tubule, filled with crystals of indigo-carmine; f, convoluted tubule, in which the nuclei have a dark color. The striations of Heidenhain are beautifully shown in the convoluted tubules. × 200. (Satterthwaite's Histology.)

Section of the splanchnic nerve, by which the kidney gets its principal nerve-supply, increases the flow of urine by relaxing the renal artery, but not to so great a degree as division of the renal nerve. As the splanchnic nerve is distributed to the whole splanchnic arcade,

the capillaries of which are dilated, the blood-pressure brought to bear upon the glomeruli does not rise so high. Stimulating the splanchnic nerve contracts the renal artery and arrests the flow of urine.

From these observations, it is quite clear that the quantity of water discharged from the kidney is governed, to a large extent, by the vaso-motor system.

The function of the epithelium, on the other hand, is much more complex; but it appears to excrete the effete material of the system, chiefly urea—the product of tissue metamorphosis.

In the experiments of Heidenhain upon the lower animals, sodium sulphindigotate, known as indigo-carmine, was injected into the blood,
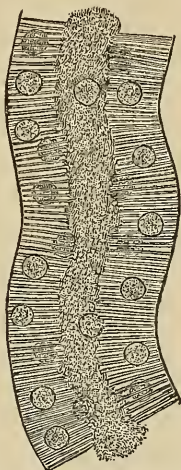
Fig. 10.—Rods of Heidenhain.

and, after the expiration of a certain length of time, the animals were killed and their kidneys carefully examined. In these experiments the indigo-carmine was found entering the epithelium through the rods of Heidenhain and passing out of the epithelium into the lumen of the uri-niferous tubules. In other experiments a length of time was permitted to elapse after the first injection, which previous experience had shown was sufficient for the complete elimination of the pigment by the epithelium. Another quantity was then injected into the blood; in this instance the elimination of the second injection of pigment was found to be incomplete, as if the cells, exhausted by their previous efforts, were unable to perform the extra work thrown upon them. Thus, so far as indigo-carmine was concerned, it was proved that, as effete material, it was eliminated by the epithelium. These experi-

ments were followed by those of Nussbaum on amphibia; the newt was the animal chosen for experiment, the kidney of which has a double vascular system—an arterial, from which the glomeruli receive their blood supply, and a venous, by which its uriniferous tubules are surrounded. These two blood-supplies have no connection, the one coming from the renal artery, the other from the bifurcation of the femoral veins, an arrangement peculiar to these animals. If one of these channels is closed, what is excreted by the other can be readily ascertained. The amount of certain substances was increased, and others not normal to the urine were brought about by injections into the systemic circulation. The result of these experiments showed that water, peptones, albumin, and sugar were found in the urine previous to the ligation of the renal artery, but that they disappeared upon the performance of the operation; urea, however, continued to appear in the urine after the artery had been tied. When indigo-carmine was injected into the circulation after ligation of this vessel, no urine was found in the bladder; but the pigment could be traced through the epithelium into the lumen of the uriniferous tubules. It appears that the excretion of water, although almost entirely confined to the glomeruli, was undertaken to a slight extent by the epithelium, probably for the purpose of dissolving the urea and rendering its excretion less difficult than it otherwise would be; but, when the additional stimulus of an increased amount of effete material excited the cells to more than ordinary action, the flow of water from them became more abundant.

Further than this, experiments have as yet shown nothing; but even these go far to prove that, in the normal state, the glomeruli supply almost if not quite all the water and inorganic salts of the urine, while to the epithelial cells lining the uriniferous tubules is left the task of excreting the products of tissue metamorphosis. By applying these physiological data to our present pathological knowledge, we are enabled to understand many conditions heretofore very obscure.

We now approach a subject concerning which there has been much uncertainty among pathologists, namely, the relation between parenchymatous change and inflammation.

In a general way, the latter may be said to include one or more of a series of changes occurring in living tissues as a result of an irritation or injury, which may be induced either by an external or an internal agency, provided the vitality of the part is not destroyed.

The exciting injury may be extrinsically direct when produced by chemical or mechanical irritants; intrinsically indirect when produced

through the blood or lymph-channels; indirect, as when internal organs become inflamed after exposure to cold. So-called idiopathic diseases, the causes of which are internal or imperceptible, come under the head of indirect, for in all cases the inflammatory process must be produced by some injury.

The usual order of events when an organ has been attacked is as follows : Acute hyperæmia—more accurately speaking, determination of blood to the part—followed by stasis; the escape of the liquor sanguinis; the migration of the white and diapedesis of the red corpuscles. Also an increase in the size and the number of the original elements, a deposit of adventitious material, changing in character the elements attacked, and death, with its necessary loss of substance.

It occasionally happens that changes in the blood and blood-vessels constitute the only signs of inflammation, as in acute meningitis, where death ensues before the exudation of all the constituents of the blood; but, for a full definition of a typical case of inflammation, all of the foregoing are necessary.

Considering all these changes essential to our conception of a true inflammatory process, it is difficult to see what relation the change called parenchymatous metamorphosis bears to inflammation.

What actually happens to the cells is that they are overworked by an attempt on their part to free the kidneys and, secondarily, the system, of an excessive amount of the incompletely formed products of tissue metamorphosis, or of some extraneous poison. The experiments of Nussbaum with indigo-carmine go to sustain this explanation. In this metamorphosis, as in his experiments, the epithelial protoplasm undoubtedly loses its power of elimination, becomes altered by the effete material, and undergoes various retrograde changes which are known as cloudy swelling, fine and coarse granular metamorphosis, and fatty transformation.

With these introductory explanations, we come to our first division of this group of renal lesions, commonly classed under the indefinite title of Bright's disease.

ACUTE PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEY.— This disease, commonly known as acute parenchymatous nephritis, is that lesion of the kidney in which the epithelial cells lining the uriniferous tubules undergo metamorphotic changes—namely, cloudy swelling and fine and coarse granular and fatty infiltration; in which, however, there is no change in the blood-vessels or interstitial tissue.

This metamorphosis occurs in connection with, or as a complication of scarlet fever, pneumonia, diphtheria, small-pox, typhus fever,

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typhoid fever, yellow fever, cholera, puerperal fever, septicæmia, pyæmia, acute yellow atrophy of the liver, rheumatism, peritonitis, meningitis, tetanus, hydrophobia, during the early stage of cirrhosis of the liver, with severe cases of jaundice, various pigmentary diseases, severe burns and following surgical operations; it may also be the result of poisoning by arsenic, phosphorus, antimony, copper, mercury, and all the potassium salts; and, in some rare cases, is said to develop without known cause. This list comprises those diseases in which the exciting cause is some original and impalpable poison which greatly interferes with the normal nutrition of the body, diminishing the perfection of its products, and increasing the amount and rapidity of their formation. The incomplete change thus produced differs from the normal physiological process in the large amount of effete material generated and the great rapidity with which it appears in the system. Great irritation is necessarily produced in the whole animal economy by the combined action of the original poison and of those incomplete products of tissue metamorphosis circulating in the blood; and to their combined action the phenomenon known as elevation of temperature is due. However this may be, the kidneys, which are the great eliminating organs of this variety of waste products, endeavor to remove from the body, by means of their epithelial cells, the irritating substances which are producing such deleterious effects upon the system. At first they may be successful, but, as the labor thrown upon them is increased, they will become exhausted (as in Heidenhain's second injection of indigo-carmine), and the process of excretion be less complete. Their protoplasm becomes infiltrated with minute particles of irritating substances, such as effete material, pigments, etc., which cause them to swell and to lose their transparency. The weakest of them undergo a progressive change which ultimately results in a complete granular or fatty metamorphosis, and a final destruction of their vital property. This process is certainly not inflammatory, but one of transformation and death, which is caused by an unduly prolonged struggle on the part of the epithelial cells to accomplish a work too great for their capacity. As the disease advances, the cells fall from their place on the wall of the uriniferous tubules, and appear in the urine as casts and cast-matter. The tubules, thus deprived of their epithelial cells, have in some places only basement membrane to form their wall; but, as only isolated cells undergo degeneration, the damage done is repaired according to the general law of regeneration and proliferation of the epithelial elements, and the wall of the tube

is restored to its normal condition after the complete subsidence of the disease, provided the chronic form is not developed.

Macroscopic Appearances.—A kidney in the condition of acute parenchymatous metamorphosis is usually enlarged, but may be normal in some few cases. The capsule is normal in thickness, does not adhere to the underlying tissue, and leaves the surface of the kidney perfectly smooth upon its removal. The cut surface in the early stage presents no marked change which can be positively recognized by the unaided eye. Later on it is pale, and the pyramids are less distinct than normal, but to the unaided eye they appear
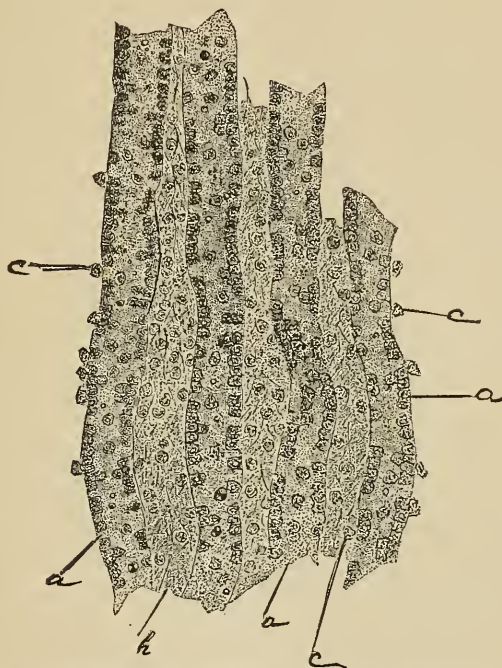
FIG. 11.—ACUTE PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEYS. × 350.

a, Uriniferous tubules showing granular metamorphosis of the epithelial cells; *c. c*, desquamated epithelial cells lying in intertubular spaces; *h*, swollen and œdematous intertubular tissue.

more distinct on account of the abnormal pallor of the cortical portion.

Microscopic Appearances.—This lesion develops four degrees of change in the renal epithelium: *First, Cloudy Swelling.*—This condition is one in which the elements are swollen by the imbibition of an albuminous fluid, and in which the protoplasm has become turbid. *Second, Finely Granular Metamorphosis.*—Here the epithe-

lium is not only cloudy, but is also infiltrated with fine granular particles, some of which are oil globules of minute size, and others granular detritus from the incomplete products of tissue metamorphosis which are in part drawn from the blood, and in part from the further destruction of the epithelial protoplasm itself. *Third, Coarse Granular Change.*—This is simply a more advanced degree of the former, with more abundant and larger fat droplets. *Fourth, Fatty Transformation.*—The protoplasm is entirely destroyed and replaced by fat globules, causing a destruction of its substance and an abolition of its function.

It seems quite probable that the cloudy and mucoid change is due to the retention of a small quantity of effete material in the protoplasm which causes this imbibition and transformation. The fine granular, too, is a further change, due to the retention of a quanity of these irritating substances now perceptible in the cell, and a commencing disintegration of the protoplasm with a development of minute fat droplets. The retention of a still larger amount of effete material produces the coarsely granular metamorphosis, or a more advanced disintegration of the protoplasm, and an increase in the size of the fat droplets. In the last (*fourth*), or fatty change, so large a quantity of the products of incomplete tissue metamorphosis, pigments, etc., remains in the cells that their normal outlines are obliterated, and the protoplasm is now destroyed by fatty degeneration.

Early in the disease, the cells having swollen rapidly, while the kidney capsule remains unstretched, the lumen of the tubules is entirely occluded, and under the microscope they are tortuous instead of straight. This, of course, refers to the straight tubules, and not to those normally convoluted; the latter, however, are considerably distorted.

In the milder forms, the change in the epithelial cells is confined principally to those of the cortical layer and those lining the glomeruli.

In more advanced cases, the cells of the pyramidal tubules also become involved. The degree of transformation of the epithelium, and the extent of territory implicated, will depend wholly upon the intensity of the cause and its duration.

After the lesion has lasted for some time, what remains of the lumen of the tubules may be found to contain single, or masses of transformed and desquamated epithelial cells, which appear like the materials from which casts are made.

Various forms of casts may occasionally be found in the lumen of the tubules.

The stroma is not involved, and the blood-vessels remain unchanged.

Symptoms.—This lesion occurring, as it does, in connection with severe diseases, or as the result of some of the acute attacks of metallic poisoning, the symptoms referable to the nephritic metamorphosis are not well marked at first.   Ordinarily, the symptoms of nephritic disease may be classified under two headings—rational, and urinary. The former are divided into cephalic, respiratory, alimentary, and general.

The cephalic are occipito-frontal headache, contraction of the pupils, injected conjunctivæ, lesions of the retinæ and optic nerves, drowsiness, convulsions, and coma.   The neuro-retinal lesions will be considered more minutely in studying those lesions of the kidneys in which they are more frequently met with, for in this form they are rarely seen.

The respiratory symptoms, which are usually asthmatic in character, are more frequently met with in the chronic forms of the disease than in the acute parenchymatous variety, and will receive more careful consideration in connection with the affections with which they are associated.

The alimentary symptoms are dyspeptic in character; they are nausea, vomiting, loss of appetite, and disgust for food, often associated with diarrhœa.

Those classed as general are œdema, commencing first in the subcutaneous connective tissue under and around the inferior eyelids, œdema of the inferior extremities, watery effusions into all the serous cavities, œdema of the superior extremities, and general anasarca. Œdema glottidis may occur.   If the disease lasts for any length of time, a peculiar waxy, almost translucent, pallor of the skin may be developed.   This, however, is seldom seen, except in that form which follows chronic metallic poisoning.

With this form a large number of the rational symptoms are masked by the severe symptoms of the disease which it complicates; but those that do attract attention are usually œdema of the eyelids and feet, undue severity of the cerebral symptoms of the primary disease, and a diminution in the quantity of urine passed *daily*.   These symptoms are followed speedily by those of a more acute character.   The patient complains of a severe headache and drowsiness, rapidly followed by convulsions and coma.   There may be associated with these cerebral symptoms, or independently, some nausea and irritability of the stomach, which often usher in severe vomiting and diarrhœa.   The œdema may now become very marked and be followed by dropsy of all the large serous cavities.   Dimness of vision may also occur in some of these cases, but is due to interference with the optic centres, and not to any lesion of the optic nerves or retinæ.   As the disease progresses,

the symptoms become more urgent, the drowsiness is followed by stupor and delirium, the urine may be entirely suppressed, and the patient·lapses into a state of coma, which is usually followed by convulsions and ·death.

During the course of the disease, which seldom lasts more than a few days, the cephalic, alimentary, and general symptoms may not be associated as above described. In some cases, especially those which occur complicating scarlet fever, pneumonia, typhoid fever, and other acute febrile diseases, only those symptoms referable to the nervous system appear, and headache, accompanied ·by dimness of vision, drowsiness, stupor, delirium, and coma follow each other in rapid succession; and, if the disease does not take a more favorable course at this point, convulsions ensue, speedily followed by a fatal result. In other cases, the alimentary symptoms present themselves, and these are most apt to terminate in chronic parenchymatous metamorphosis, resulting, as they do, from the mineral poisons.

Urinary symptoms are always present in all forms of the disease. The urine is always diminished in quantity, high-colored, and its reaction acid; the specific gravity ranges between 1.020 and 1.030, but when the quantity passed is considered as compared with the normal daily quantity, the specific gravity is found to be below the normal. Albumin is always present, sometimes in great quantities, sometimes only a trace, or to the amount of one or two per cent, by volume; while in the most severe types of the disease it may completely solidify the urine when boiled, so that, if the test-tube is inverted, no water flows away.

On microscopical examination early in the disease, small hyaline, epithelial, nucleated, and fine granular casts and granular *débris* are seen, while at a later stage the coarsely granular and fatty casts make their appearance; and as the disease advances, the casts increase in size.

The *diagnosis* is readily made by remembering the causes, and by a careful examination for casts. The only disease for which it might be mistaken is acute diffuse nephritis. In the latter we find blood and blood-casts in the urine; but in this lesion they do not occur.

The *prognosis* is always grave, and especially so when the lesion exists as a complication of acute disease. In scarlet fever, if convulsions occur, the patient rarely, if ever, recovers; while in pneumonia, diphtheria, typhoid fever, etc., the first symptom of acute parenchymatous metamorphosis renders a favorable termination very doubtful,

although there are instances in which patients recover even with this severe complication.

In those cases which result from mineral poisoning, the immediate danger is not so great; but the disease is very apt to lapse into the chronic variety, which may end fatally in the course of a few years.

In *treating* this lesion, its method of production should be kept constantly in view. It should be remembered that it is not of an inflammatory nature, but that it results from too much work being thrown upon the kidneys which undergo this metamorphosis through their efforts to relieve the system. With this light upon the subject, the great object in the way of treatment is to prevent an excessive amount of work being forced upon these glands.

There is no doubt that elevation of temperature or heat, as the damaging element in disease, has been much overestimated, and the *cause* of the increased heat been too much neglected. The increase of body-heat should only be looked upon as a *symptom*, produced in part by the irritation of the original poison, and in part by the too abundant and incomplete products of tissue metamorphosis, which are excited by the poison and which circulate throughout the system.

All we can do in reference to neutralizing the original cause is to make the hygienic surroundings as perfect as possible, and to supply the patient with a large quantity of fresh air.

The original poison, in a measure, is probably eliminated from the system by the kidneys, and also aids in damaging the epithelial protoplasm.

With such a condition as this, the kidneys make an effort to rid the system of this excessive amount of effete material, while at the same time they receive less nutriment than in health, and, consequently, are very likely to suffer irreparable damage.

The application of cold to the body in such conditions as these, according to well established physiological laws, still further interferes with tissue metamorphosis and adds new fuel to the fire. Many cases have undoubtedly developed a fatal renal complication in this way. It often happens that, following a cold pack or bath, the cerebral symptoms increase in severity, the temperature rises higher, and albumin presents itself in the urine for the first time; a speedy and fatal termination soon following by an induced renal complication. A striking example of this kind was observed in a case of *sunstroke*. In this case, at the commencement of the attack there was a trace of albumin in the urine; but, following the repeated application of cold to lower the temperature, the quantity of albumin rose to 50 per cent by volume, and all the urinary symptoms of acute parenchymatous

metamorphosis presented themselves. Subsequent post-mortem examination confirmed the diagnosis in regard to the renal lesion. Remembering these facts, the kidneys should demand our first attention in all these severe diseases and in cases of acute metallic poisoning. Every effort should be made to aid the kidneys during this severe strain and to guard them against this transformation, not waiting until the metamorphosis has actually developed and then try to cope with so formidable a malady.

In these cases our attention should be directed to the other excretory channels—namely, the skin and alimentary tract—and every effort should be exerted to cause them to perform the largest possible amount of work. By so doing, we relieve, to a considerable extent, the increased strain upon these organs.

Cold applications to the skin should be avoided, but it should be kept moist and active by bathing in tepid water, or with tepid water to which a little alcohol has been added.

In bathing the sick, one rule should be rigidly enforced. After sponging a portion of the body, the nurse should rub the skin of that part perfectly dry with the bare hands before another portion is bathed. There is nothing more uncomfortable than to be left wet and clammy. On the other hand, nothing is more refreshing and soothing to a patient than such a bath, provided the skin is dried in the way here suggested. The skin is also rendered more active—one great object to be attained.

Diaphoretics may also be used to advantage; jaborandi, or its alkaloids, standing first upon the list for promptness and certainty ; but in these severe forms of disease its use would be contra-indicated, as it is sometimes said to be depressing in its effects. The liquor ammoni acetatis, or spiritus ætheris nitrosi, may be found serviceable in keeping up free activity on the part of the skin.

Alcohol, which is often called for in these febrile diseases, acts as a diaphoretic and diuretic ; it also retards oxidation, thus being of service in three ways.

The bowels should be acted upon as freely as the pre-existing condition will admit. In typhoid fever, little can be accomplished in this direction; excepting in this fever, yellow fever, and cholera, they should be moved at least once every day.

Treatment referable to the kidneys is of the greatest importance. The main object is to increase the watery constituents to the maximum, so that the effete material necessarily passing through the renal protoplasm shall be diluted as much as possible.

To accomplish this object, large draughts of water, demulcent

drinks, and various mild mineral waters should be freely administered.

As medicinal diuretics, tinctura ferri chloridi, digitalis and its preparations, are the only ones to be used. The tincture of iron is an invaluable remedy, acting as a non-irritating diuretic, and enabling the blood to carry more oxygen, thus aiding in bringing about a more perfect tissue metamorphosis. It is most serviceable as the disease advances, and tends to assume a more persistent form.

Digitalis and its preparations as diuretics are serviceable remedies during the early stages of this lesion. They are non-irritating, and act principally by contracting the arterioles and increasing the general blood-pressure; in this way increasing the pressure upon the glomeruli. They probably have less effect upon the renal arterioles than on the rest of the circulatory system, otherwise they would diminish instead of increase the flow of urine. Further investigation will probably show that they only act when there is venous congestion of the intertubular plexus of veins. Some have advanced the idea that this drug has a specific, and as yet unexplained, action directly upon the kidneys, especially upon the Malpighian tufts. The condition of the intertubular plexus may be the cause of the so-called specific effect.

The potassium salts are contra-indicated as diuretics, as they depress the heart's action and relax the arterioles. Their action as diuretics is ascribed to their power to increase oxidation and tissue metamorphosis, and in this way force more work upon the renal epithelial cells. They are therefore injurious for three reasons : *First*, they weaken the heart ; *second*, they relax the whole arterial system ; and, *third*, they increase the effete material to be thrown off by the epithelial protoplasm.

When opiates are used as nerve-sedatives, in this form of renal lesion, a fatal termination often results, if it is not the rule. In some forms of acute uræmia, morphine, hypodermatically administered, may be efficacious, but is not considered safe.

The application of dry cups to the loins, followed by warm poultices, will be found very serviceable, especially if the renal symptoms become at all severe.

The functional derangement of the liver, with its inability to produce a sufficient quantity and quality of bile to prevent the decomposition in the alimentary tract, and assist in perfecting the intestinal and hepatic digestion, requires a word in connection with the treatment.

Recent experiments go to show that all infectious diseases produce

as their first effect a disturbance in the bile-producing power of the liver.

With this condition the intestinal and hepatic digestion is very imperfectly performed and its products are quite incomplete and irritating, which, together with the constantly absorbed decomposing materials from the intestine, are the chief causes of the increased bodily heat, and of the overworking of the kidneys.

This condition may be overcome in a large measure by using the pure or inspissated ox bile, either alone or in combination, as in the following formula :

℞ Fellis Bovis Inspissati, . . . ℨ ss. 3.7 grams.
Quininæ Sulphatis, . . . gr. xv. 0.9 grams.
Extracti Taraxaci, ... ℨ ss. 3.7 grams.

M. et fiat massa las in capsulas no. xv. dividenda.

Sig. One *ter in die*, or every three hours, as the case may require.

The ordinary pure ox bile may be given in drachm doses, or the inspissated in doses of two or three grains.

By either method, the decomposition going on in the intestinal tract is overcome, and digestion, absorption, and assimilation become more perfect, while the liver is supplied with new bile with which to do its work.

As a result the temperature falls, the products of tissue metamorphosis to be eliminated are diminished in quantity and rendered more perfect and less irritating to the excretory organs; consequently the work to be accomplished by the renal epithelium is decreased and it is enabled to maintain its integrity and repair the damage it has received.

CHAPTER III.

CHRONIC PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEYS.
PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEYS ASSOCIATED WITH PREGNANCY. PARENCHYMATOUS INFILTRATION
OF THE KIDNEYS ASSOCIATED WITH WASTING DISEASE.

Chronic Parenchymatous Metamorphosis of the Kidneys.

FIRST FORM OF LARGE WHITE KIDNEYS.

Definition.—Chronic parenchymatous metamorphosis of the kidneys
is a transformation in which the irritation of the epithelial cells
lining the uriniferous tubules has continued for a considerable
length of time, and caused a progressive granular and fatty change.
The slight alteration in the intertubular tissue is œdematous in
character and not inflammatory.

Etiology.—A large number of the cases appear to result from
a previous acute attack which has passed without being recognized,
and it is often associated with cirrhosis of the liver and with all forms
of chronic hepatic disease which disturb the functions of the liver
so that the transformed proteids are less perfectly formed and produced in abnormally large quantities. As a result of this condition,
the kidneys attempt to rid the system of the effete material, and
the substances which have now to be eliminated by the special renal
epithelial cells are not only more abundant, but unduly irritating.
For a time, however, the kidneys may succeed in performing this
extra work, much of which should have been accomplished by the
liver, without suffering any material change, but, ultimately, the
cells give way and the abnormal condition is fully established.

In connection with acute diseases there is a similar transformation,
only of a more acute nature, which results in an arrest of the metamorphosis, and a restoration of the renal cells to a fairly normal
condition upon the removal of the cause, that is to say, upon recovery
from the condition which gave rise to the morbid phenomena. The
kidneys, however, remain somewhat damaged and consequently more
susceptible to a second attack, or later on in life to a spontaneous de-

velopment, as it were, of this metamorphotic change, which then assumes a chronic type. It is in this way that many of the chronic cases have their origin.

Repeated attacks of acute diseases, with their accompanying changes in the overworked renal organs, must in time impair the renal cells to such an extent as to place them beyond hope of repair. These attacks decidedly damage the excretory function of the glands, and as a person advances in years this form of chronic renal lesion is more likely to be developed. These mild, but many times repeated and often unnoticed attacks of acute metamorphosis are the most potent predisposing causes for all forms of chronic nephritic diseases commonly classed as Bright's.

Until this fact is more fully appreciated, and the renal cells more carefully guarded, when subjected to such extra strains, chronic renal lesions will remain common.

By carefully considering the way in which these lesions originate, most of the so-called idiopathic cases can be traced to some definite origin. Overcrowding patients with food and stimulants beyond the capacity of the liver undoubtedly is a very common cause of this chronic type. In the early stage of either form, if the cause can be removed, it would seem reasonable to suppose that here, as elsewhere in the body, the epithelial cells would proliferate and fill up the gaps left by those that have already fallen from their places.

In many instances this is the case, especially in the acute variety; but in some, another influence appears in the form of an unobserved irritant, which, by being continually applied to already weakened cells, prevents their complete regeneration and causes a subacute which finally develops into the chronic condition. Before the attack of the originating disease, the epithelial cells of the kidneys have no difficulty in removing from the circulation those effete materials which it is their function to excrete; but the acute attack of parenchymatous metamorphosis lessens their number and quality to a very great extent, so that even where the general system has returned to its original state, the remaining cells, already in a damaged condition, are called upon to perform the work which was previously accomplished by a much larger number. An important question now arises: will this small number of weak cells be capable of removing the products of normal tissue change which are circulating in the blood, and at the same time regain their own normal condition ? If so, they will proliferate and renew the epithelial lining of the tubules, and the kidney will be restored to a perfect physiological state; if not, they will tend to undergo further retrograde

change, and as healthy tissue cannot be built from unhealthy, no new cells capable of performing the functions of the old will be produced, and the remaining corpuscles will be more and more transformed. These in turn finally degenerate, drop from their places, and leave the kidneys wholly unable to perform their task, even though they are aided in every way possible, by increased action of the skin and bowels. In continued and often repeated exposure to cold, and in failure in the functional activity of the liver, the effete material in the circulation is considerably increased and less completely transformed, although not to so great an extent as to produce an acute parenchymatous change in the kidneys, but still sufficient to bring about a subacute condition; and, now, if the over-worked cells are not quickly relieved from this extra strain, they undergo the further retrograde change, and the patient eventually succumbs.

Renal lesions dependent upon the excessive use of alcohol as their etiological factor are produced in like manner, instead of depending for their cause upon any direct irritation of the renal tissue *per se,* and when the trouble dates from the ingestion of a metallic poison, it takes first the acute and subsequently the chronic form.

Pathological Anatomy.—The kidneys are always enlarged, and their capsules are normal in thickness, and non-adherent to the underlying renal tissue, which is usually smooth after enucleation. If the disease has been of considerable duration, there may be some slight adhesion of the capsule to the gland. The cut surface may show the cortex and medullary portion to be paler than normal, but to a trained eye both have a granular and fatty appearance. The cortex is several times thicker than usual, the markings are straight, and the Malpighian pyramids distinct. In the gross anatomy, these markings are very diagnostic points. If they run perfectly straight from the base of the pyramids to the surface of the kidneys, they indicate that whatever change exists is almost exclusively confined to the epithelium; but when they are found to be wavy or tortuous in their course, they indicate that there is also an interstitial change. It is the development and irregular contraction of the newly-formed connective tissue that causes this wavy appearance, which is found in the chronic, diffuse, and sclerotic, but not in the parenchymatous forms of kidney lesion.

Microscopic Examinations.—When thin sections are examined, the epithelial cells are seen to be swollen, and to have undergone an extensive granular and fatty metamorphosis; and in aggravated cases of long duration, there is a slight thickening of the interstitial tissue and of Bowman's capsule, which has the appearance of being œdema-

tous rather than a true inflammatory proliferation. Some sections
will show the tubules partly filled with desquamated epithelial cells
and casts. Some observers, from the slight adhesion of the capsule
and apparent swelling of the intertubular tissue might be inclined to
class this as a diffuse nephritis, but as the primary and principal
lesion is in the epithelial cells, while the interstitial change is slight,
secondary, and not inflammatory, it should be regarded as only a
parenchymatous metamorphosis, for the causation, pathological ana-
tomy, and symptoms are decidedly different from those of chronic,
diffuse, and inflammatory lesions of the kidney. In some, if not
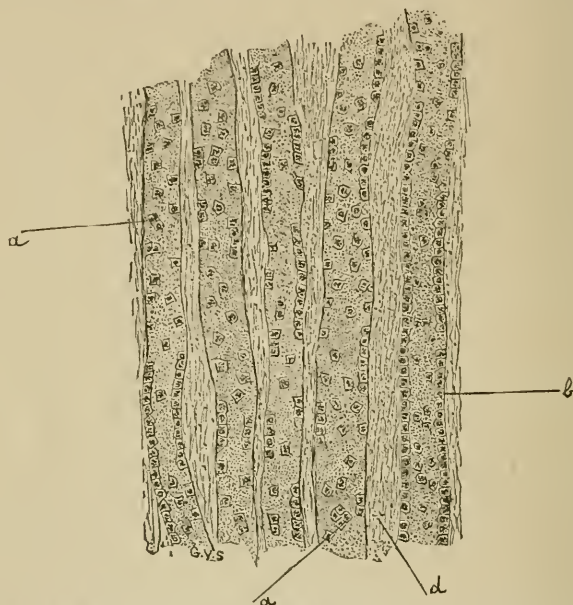
Fig. 12.—Chronic Parenchymatous Metamorphosis of the Kidney. ×350.

a, Tubules showing epithelial cell in a state of granular transformation and desquamation; b,
tubule showing less marked change; d, œdematous intertubular tissue.

in all, the epithelial cells lining the uriniferous tubules undergo,
so to speak, a peripheral molecular death or solution of continuity,
analogous to ulceration in the soft parts. The irritating pigment par-
ticles and granules from the degenerating epithelium become attached
to or imbedded in the hyaline substance which is poured into the
lumen of the tubules, and forms the basis for casts. By the amount
and size of the granules, the different grades of casts are formed.
The most frequent way in which granular casts are formed is by the
degeneration, desquamation, and attachment of such cells to this

hyaline plug.   A close examination of a hyaline cast which appears a little granular will almost always show upon its surface the faint outlines of what was once epithelial cells.   Some believe that this hyaline substance undergoes disintegration, but, as it is generally regarded as fibrinous in nature, this seems impossible.   In other cases, the epithelial cells desquamate in the various stages, and become agglutinated together, thus forming casts without the intervention of the hyaline plug.   The majority, however, are produced in the former way.

Symptoms.—The early clinical manifestations of this disease are not well marked, and the lesion has usually existed for some time before it is discovered.   The first symptoms to attract the patient's attention are headache, loss of appetite, nausea, and occasional vomiting.   These, however, are not persistent, but come and go from time to time.   There is a diminution in the quantity of urine passed, which may attract attention.   Œdema next appears, and is a very marked and constant symptom, commencing first either in the subcutaneous areolar tissue in and around the inferior eyelids, or about the feet and ankles, but usually in the former situation.   The areolar tissue of the limbs, and especially of the legs, is soon filled with serum; the scrotum becomes dropsical, so also the peritoneal and pleural cavities, the face has a pale and puffy look, health and strength rapidly decline, and, upon slight exertion, the patients feel completely exhausted.

The blood undergoes a change, becoming thin and watery, which causes the skin to assume a peculiar pale, waxy, translucent hue, characteristic of renal lesions.

These symptoms continue for several weeks, or even months, and may be continuous or intermittent in character.   After a time, the dropsy increases so as to interfere greatly with respiration, the dyspnœa being very marked, on account of the diminished chest space, and the interference with a free expansion of the lung, by the effusion into the pleural cavity, and the crowding up of the diaphragm by the fluid in the peritoneal sac.   The dyspnœa may also be due in part to an incomplete oxidation of the blood, owing to its watery condition, and in part to the cerebral irritation brought about by the action of the effete materials retained and circulating in the blood.   Occasionally there is dimness of vision, which is generally cerebral in origin, and not due to any lesion of the optic nerves or retinæ.   This lesion is not a marked or common complication.   As the disease proceeds, frequent attacks of nausea and vomiting occur.   The cerebral symptoms are not very prominent until towards the last,

when what headache there may have been gives place to drowsiness or stupor, partial loss of memory, followed by a low muttering delirium, rise in temperature, dry skin, muscular twitchings, convulsions, and a urinous odor emitted from the body, followed by contraction of the pupils, coma, and death from uræmia.

Other cases seem to die from simple exhaustion without any of the active symptoms of uræmic poisoning. A sudden effusion of serum into the pericardial sac may cause paralysis of the heart, and act as the immediate cause of death.

Urinary Examination.—In this lesion, the daily quantity of urine passed is diminished, varying from ten to thirty ounces; its color is darker than and its specific gravity above the normal, ranging between 1.018 and 1.030, and the quantity of albumin varies, but is usually abundant.

Microscopical Examination.—Casts are very numerous, and of the large hyaline, coarsely granular, and fatty varieties, the two latter predominating. There is a large quantity of *débris* in the field, which is cast matter, or degenerated and desquamated epithelial cells. A few red blood-corpuscles and leucocytes are usually present, but no blood casts are found. Renal, bladder, and vaginal epithelial cells will be found in some of the specimens.

Diagnosis.—This is readily made by remembering the cause and the general symptoms, taken together with the *urinary analysis.* The small quantity of urine passed daily, the high specific gravity, the abundance of albumin, and the great number of large hyaline, granular and fatty casts and cast *débris* are diagnostic. It is only by a thorough microscopic analysis of the urine that anything like accuracy in diagnosis can be attained in this or any other form of renal disease.

There is no other kidney lesion for which this form could be mistaken, if the above facts are carefully remembered and applied. A positive diagnosis should never be attempted, however, until several samples of urine have been carefully analyzed.

This variety, as a separate and distinct lesion, is quite common, but it has been often confounded with the chronic diffuse variety. The fibres of the tissue are swollen, boggy, but not studded with inflammatory corpuscles.

From the method of production, the character of the lesion, and the distinctiveness of the clinical and urinary symptoms, all of which differ from those in chonic diffuse nephritis, it should be regarded as a chronic parenchymatous metamorphosis, and not as a diffuse nephritis.

Prognosis.—The duration is variable, it may last only a few weeks, or it may exist for several months; possibly for one or two years, but the longer duration is extremely doubtful. If the disease is recognized and accurately diagnosticated at first, there may, with proper treatment, be some prospect of a favorable result, but the majority of cases even then will terminate in an early death. It seldom happens that a patient completely recovers; an apparent recovery may result, and all the symptoms disappear for a time, but they are almost certain to return and finally to cause a fatal termination. One attack predisposes to another, and if once confined to bed, there need be little thought of recovery. Strictly speaking, this lesion is neither rapid nor slow in its progress, but when we carefully consider its etiology, its fatality is easily undertood.

Treatment.—This is governed by the same laws as in the acute form. The primary effort should be to remove the cause. This can be accomplished in a great measure by preventing the development of the acute form, by a guarded use, or better still, a total abstinence from alcoholic beverages, and a scrupulous avoidance of all agents which are damaging to the *hepatic* function. The only reason why the damage is not developed sooner by alcohol may be explained by the marked diminution in oxidation attributable to the alcohol, and also the large amount of fluid usually taken in conjunction with it, which, being eliminated by the kidneys, relieves to some extent the strain upon these glands. But for these conditions its action would be more damaging. Exposure to sudden changes in temperature should be carefully guarded against.

Unfortunately, most of the circumstances which tend to produce this lesion are to a considerable extent beyond the control of the physician, who is generally called to deal with the fully established lesion, and about all he can hope to accomplish is to stay the progress of the disease, and to ward off the fatal issue as long as possible.

All through the course of the disease, the diet should be carefully regulated.

Believing that this lesion is produced by overwork, possibly associated, as some have suggested, with a deficient eliminating power on the part of the skin and alimentary tract, the first object should be to see that the food is easily digested, absorbed, and assimilated, and to recommend that which will ultimately give the smallest and most completely formed excretory products. By so doing we remove the strain upon the renal epithelial cells to a considerable extent. A milk diet, or one limited to skim milk alone, when it can be borne, ranks first upon the dietary list. The only therapeutic value

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which can be attributed to milk is its diuretic property. Food of all kinds should be limited to plain nutritious substances, not highly seasoned. Some advise a diminution in meats or a complete abstinence from them.

All kinds of food should be taken with moderation; great care being exercised not to over-eat. Experience teaches that fats and starches are more deleterious than the purely albuminous articles. The system may be sufficiently strong to digest and improve upon a purely nitrogenous diet, but the addition of the non-nitrogenous articles interferes with perfect digestion. The latter being more easily assimilated, tire out the system and render it incapable of digesting the proteids which are to follow, and the usefulness of both is thus impaired. It appears to be in this way that the harm comes from a mixed diet.

The taking of more food than the system absolutely requires must of necessity act as an irritant, and, in a lesion like this, renders the condition much worse. All forms of rich and greasy food and pastry should be absolutely withheld.

In regard to the curative efficacy of tonics, there is much diversity of opinion. There can be little doubt, however, that they are of value in so far as they tend to improve the digestive and assimilative processes, and render the tissue metamorphosis more complete and less irritating. The tincture of the chloride of iron stands first, from its action both as a diuretic and a carrier of oxygen. An almost innumerable list of drugs and mineral waters have been extolled for their curative properties, but there has been no one remedy or series of remedies discovered as yet, whose curative action can be looked upon with any degree of certainty. It is hardly to be expected that any single remedy will be found that will be capable of removing the causes and at the same time of repairing the damage already done to the tissues. No specific virus can be found that will prove antidotal to these causes. The great object naturally is to reduce as far as possible the intensity of the irritation which the renal epithelial cells are continually suffering. If the cause cannot be completely overcome, the skin and bowels should be kept active, the liver free from over-pressure, and the nutrition as abundant and as perfect as the demands of the system require. In this way the best conditions for recovery are instituted and sustained, and nature has an opportunity to repair the damage inflicted.

An exclusively " diaphoretic treatment," as it has been called, or one limited solely to the alimentary tract, should be avoided and con-

demned; but by aiding all the excretory organs in every known way, their work will be accomplished in the shortest space of time, and with the least strain. This should be the main object, because it gives the longest interval of repose, and allows more time for repair.

The three things to be guarded against particularly are, the accumulation of effete products in the blood, their deleterious effects upon the system, and uræmia.

Diaphoretics.—These agents are of great service, with jaborandi and its alkaloids standing first. In regard to this medicinal agent, much has been said *pro et con.*, and in lesions of this type it has been used with varying doses, some claiming that it has a depressing, others that it has a stimulating influence upon the heart, but the truth is that in small quantities it appears to depress, and in large doses to stimulate that organ. From observation in many of the cases upon which this chapter is based, only one conclusion can be deduced, namely, that in most instances the quantity administered is too small. The dose, as commonly given in most of the works on therapeutics, is from one-fifth to one-half a grain of pilocarpine. In all the cases from which these conclusions are formulated, the drug was always given by subcutaneous injection, and the smallest amount ever administered was half a grain of the muriate of pilocarpine. This preparation is preferable to the nitrate or sulphate, and with this dose the effects were not very marked; but when the quantity was raised to two-thirds or three-fourths of a grain, the most desirable results were obtained.

In one case, where the patient was suffering from very severe and rapidly recurring uræmic convulsions, and was almost "water-logged," two grains of the muriate of pilocarpine were hypodermatically injected, followed at a short interval by another grain administered in the same way. The result was more than could be expected from any human agency. At the time the urine was nearly suppressed, and for weeks before, there had been a diminished quantity, heavily loaded with albumin and containing large numbers of casts.

The convulsions and coma gradually wore away, the œdema partially disappeared, and consciousness returned, so that for eleven days the patient was fairly comfortable. On the twelfth day she died from exhaustion, *without a recurrence of the convulsions.* The patient had repeatedly taken three-quarters of a grain without any ill effects. When under the influence of the pilocarpine, both ammonia and alcohol were given freely, as both pleural sacs and the pericardium contained fluid.

A patient who was treated in this way, first at the college clinic, and later at his home, by one of the assistants, after being put under the influence of three-quarters of a grain, exclaimed, " O Doctor, this is paradise !" thus conveying a vivid impression of the relief he had obtained.

In many instances the pilocarpine is substituted after elaterium, croton oil, etc., have failed and before the system has recovered from their effects. Under such circumstances, when reaction commences, a depressing effect must be expected.

Continued observation has failed to reveal any case where there was evidence of a depressing effect from the use of this drug, but owing to the fact that the opposite has been reported, it is always well to give some ammonia or alcohol, or both, in *advance* of the pilocarpine.

The hot-air bath may be resorted to, but as a rule it is more depressing than pilocarpine. If the patient be able to sit up, a blanket may be thrown around the body and chair in which he is sitting, and a tripod holding a dish of water, under which a lighted alcohol lamp is placed, may be put under the chair. In case the patient is confined to bed, a frame may be placed over the body, and by means of a tin tube, curved so as to project underneath the bed clothing, the space around the body may be heated, by an alcohol lamp placed in the tube, near its lower extremity. The air in this case can be moistened by the use of an evaporating dish. Moist air is less depressing than dry.

Diuretics.—Here, as in the acute variety, the only safe diuretics are, the tincture of the chloride of iron, digitalis, and caffeine. The digitalis acts by contracting the arterioles throughout the body, in this way increasing the blood-pressure upon the coil of vessels constituting the glomeruli; it also acts as a powerful diuretic only when there is congestion of the intertubular plexus, obstructing the escape of blood from the glomeruli.

The combined diuretic action of digitalis, caffeine, and strychnine, in pill form, will often be found serviceable; each pill should contain three grains of caffeine, one grain of powdered digitalis leaves, and one-twentieth of a grain of strychnine. The potassium salts should *never* be used, for the reasons mentioned on page 25.

The application of dry cups to the loins, followed by warm poultices, will be found useful, and often will increase the diuretic effect of the digitalis.

A free use of mineral waters, by increasing the amount of water to be eliminated, keeps the tubules well washed out and free from casts and débris.

Ordinary coffee will also act as a diuretic, both from the bulk of fluid and the contained caffeine, and it also tends, like caffeine, to lessen tissue waste and to stimulate cardiac contraction.

Caffeine has been recommended alone, as a diuretic in renal as well as in cardiac dropsy, but from the general impression that it will produce severe cerebral symptoms it has not come into general use.   The above pill acts well, and does not produce any undue cerebral excitement.   Caffeine should *never* be used in conjunction with pilocarpine, as the most alarming, if not fatal, symptoms are likely to occur.

Cathartics are sometimes called for, especially if there is a tendency to uræmic symptoms with excessive and persistent œdema.   The most efficacious cathartic is elaterium in small and repeated doses. If the œdema of the lower extremities is excessive and troublesome, and does not yield to ordinary treatment, it may in some cases be desirable to incise the integument, and also administer diuretics in moderation.   Several small incisions, one-half to one inch in length, should be made around each ankle and warm fomentations should then be applied, or the limb soaked in warm water.   Some advise numerous small punctures instead of the longer incision, but the former is generally considered the better method.   The objection to this is that occasionally an erythematous inflammation is developed, which, in some cases, is only an erythema, but occasionally it develops into a true erysipelatous inflammation which often terminates in extensive sloughing or gangrene.   After the dropsy has been overcome in this way, it can be easily controlled by well-directed methods.

Another very reliable method of removing the dropsy of the extremities is by the use of *Esmarch's bandage*.   If at night the limb be firmly bandaged with the rubber roller, the water will be driven up toward the trunk and the pressure in the abdominal vessels will be greatly increased.   Having accomplished this, the œdema can be made to rapidly disappear, by the free use of hydragogue cathartics and diuretics.   By repeating this for several nights, excessive and troublesome œdema, which has resisted all other lines of treatment, can be overcome and held in check for a long time.   Ten grains each of calomel and jalap is the best cathartic at this time, or the compound jalap powder.

Parenchymatous Metamorphosis of Pregnancy.

SECOND FORM OF LARGE WHITE KIDNEY.

Etiology.—During pregnancy, the kidneys are liable to undergo metamorphotic changes. Although histologically this lesion closely resembles the last forms, it is classed as a separate lesion, from the fact that its cause is definite, its treatment special, and that, with the removal of the cause, the natural tendency is towards a spontaneous recovery. At first it is similar to the acute parenchymatous metamorphosis, but later it becomes chronic.

It has for its cause the general nervous irritability incidental to the pregnant state, which has a tendency to interrupt the physiological metamorphosis and render its products imperfect and irritating to the system and excretory organs. There is also increased work demanded of the renal glands, as they have to eliminate the effete products of both mother and fœtus. At the same time the nutrition of the renal organs is impaired, first, by the general disturbance to the abdominal circulation, and, later on in gestation, by direct pressure upon the renal vessels.

Pathological Anatomy.—The kidneys are usually large than normal, never smaller; their capsules are non-adherent to the underlying renal surface which is smooth.

The external and cut surface is pale, the whiteness of the cortical substance being more marked than that of the pyramids which are quite distinct.

Upon *microscopic examination*, the various degrees of retrograde metamorphosis known as cloudy, mucoid, and finely granular or fatty transformation are found, this depending upon the stage of the disease (see Fig. 11, p. 19). But as death occurs most frequently during the latter months of pregnancy or after delivery, the changes most commonly seen are those of the coarsely granular and fatty metamorphosis, chiefly the former (see Fig. 12, page 30). The fibrillated connective tissue and Bowman's capsule have a swollen and œdematous appearance, which appears to partake more of a passive than of an active or inflammatory nature.

This lesion is progressive from the acute to the chronic form.

Symptoms.—The disease may develop at any time during pregnancy, but it usually makes its appearance during the latter months when there is often great difficulty in ascertaining whether some of the symptoms are due to the pregnant condition, to the parenchymatous metamorphosis, or to both. Occipito-frontal headache and œdema of

the eyelids may become quite marked, and dimness of vision is also often present. Œdema of the feet, dyspnœa, and derangement of digestion are almost always seen during pregnancy, and, therefore, these symptoms must not be too positively relied upon as symptoms of parenchymatous metamorphosis, as in other cases they would be.

As pregnancy and the disease advance, the quantity of urine voided becomes much diminished and pale in color; it may even be suppressed; the dimness of vision increases, and the patient becomes very restless; these symptoms usually occur during the eighth or ninth months, but they may appear earlier.

If the *urine* is examined at this time, its specific gravity will be found to be a little above normal, albumin will be abundant, and the color will be slightly deeper. But finally the specific gravity falls, and the color of the urine is abnormally pale, resembling that of the chronic diffuse forms. This is explained by the rapidly progressing hydrœmic condition of the blood associated with pregnancy.

Upon *microscopical* examination, casts of all varieties, except blood, are found; the size of the casts varying with the different stages of the disease. A few red blood-corpuscles and leucocytes may be found in some samples, but these usually come from various portions of the genito-urinary tract and do not indicate a renal hemorrhage. The symptoms of uræmic poisoning soon become quite marked, the patient is very nervous and anxious, and may become almost delirious.

The pulse is rapid, compressible, and very weak. In some cases, these symptoms may not progress further, but in others, if not relieved, they are rapidly followed by convulsions and death. The convulsions may not appear until excited by the pains of pregnancy, when they make the labor doubly difficult and dangerous.

Prognosis.—Occurring at such a time, this disease should be anxiously watched by the physician; for it may of itself produce abortion or a premature expulsion of the fœtus. If the convulsions occur before or during labor, the patient's life is in great jeopardy and the prognosis is serious, though not necessarily unfavorable. If the convulsions do not come on until after labor has been accomplished, the prognosis is much more favorable, for the cause of the disease has been in a great measure removed; and if the patient can be relieved from the immediate danger, she usually makes a rapid and perfect recovery. When the disease is not so severe, and only some nervousness and anxiety are present, together with only a moderate amount of albumin and the urine not much diminished in daily quantity, the prognosis is favorable, but the patient should be carefully watched.

This variety of renal lesion shows quite conclusively that the epithe-

lial cells of the kidneys can and do undergo a marked degree of retro-
grade change, after which they may be restored to their normal con-
dition. The essential thing, however, is a speedy removal of the
irritating agent.

Treatment.—Owing to the condition of the patient, the treatment
for this disease cannot be so active as in other cases of renal disease.

As soon as the kidney complication is discovered, mild hydra-
gogue cathartics, such as jalap and calomel in doses of ten grains each,
must be given as often as is necessary to keep the bowels freely
open; dry cups, sinapisms, or hot poultices should be applied over
the loins, together with the internal administration of the infusion of
digitalis ℥ ss. (1.85 grams) *ter in die.* This will often improve
the condition of the kidneys by lessening the congestion and by
increasing the amount of urine excreted. In using the cathartics,
great care should be exercised not to produce uterine irritation and
premature delivery.

The action of the skin may be promoted by the vapor-bath, hot
wet packs, and diaphoretic medicines, as jaborandi gr. xx. to xxx.
(1.29–1.94 grams) or by the following:

R Liquor. Ammonii Acetatis. .... ℥ iss.
   Spiritus Ætheris Nitrosi........................ ℥ vi.
   Tincturæ Ferri Chloridi......................... ℥ ss.
   Aquæ..................................q. s. ad ℥ vi.

M. Sig. One-half ounce every three hours in a wineglass of water.

The potassium salts should always be avoided, for the reasons given
when speaking of the acute parenchymatous metamorphosis, page 25.

The food should be carefully regulated, and all indigestible sub-
stances stricken from the dietary.

If the patient be anæmic, iron should be given. In plethoric pa-
tients, venesection should be performed, and even in anæmic patients,
if the physician thinks convulsions probable, the operation will often
be followed by good, and seldom, if ever, by bad results. The amount
of blood to be drawn should not be more than sixteen ounces; usually
much less, but this depends entirely upon the patient's strength. If
none of the above methods be successful, premature delivery should be
induced. Should convulsions occur, bleeding is indicated as soon as
the fit is over, if it has not already been done. Morphine gr. ss.
(0.032 gram) may be injected hypodermatically and is followed by the
most pleasing results; chloral hydrate gr. xv. (0.9 gram) or bro-
mide of potassium gr. xxx. (1.9 grams), either alone or combined,

may be given by the mouth or rectum; the best results will be obtained from their combined action.

Ether or chloroform may be given to prevent the return of the convulsions, but at the same time it should be remembered that chloroform is not absolutely safe even here. The patient should be delivered immediately. The hot wet pack, even at this time, is of service and does not interfere with delivery.

As a rule, pilocarpine has not been considered safe in this lesion, but what has already been said on page 24 applies equally in this condition. It will undoubtedly cause a rapid expulsion of the child, which is apt to be still-born, but it will often save the life of the mother.

The method of production being clearly understood, much can be accomplished in the line of prevention and more active symptoms obviated. The bowels should be kept free and the skin active. Especial attention should be paid to the gastric, intestinal, and hepatic digestion, that their functions may be as nearly normal as possible ; in this way nutrition may be kept at the highest standard attainable, and the excretory products reduced to the minimum both in quantity and irritability.

By accomplishing all this, the pregnant and puerperal state, which otherwise might terminate in the death of both mother and child or, to say the least, with alarming symptoms in the former and death of the child, may be carried to a successful termination without uræmic symptoms, and with the delivery of a strong and vigorous infant.

Parenchymatous Infiltration Metamorphosis of the Kidney with Wasting Diseases.

THIRD FORM OF LARGE WHITE KIDNEY.

Definition.—Chronic parenchymatous infiltration metamorphosis is, more strictly speaking, a passive lesion similar to the fatty liver of phthisis and other wasting diseases. In this form, the epithelial cells become swollen and pale from the continued imbibition of fatty particles, which do not irritate the cell protoplasm sufficiently to prevent the performance of its function. It is only classed among the renal lesions on account of its gross appearances, being so nearly like those of the more active type.

Etiology.—It occurs in connection with phthisis, carcinoma, and all forms of wasting diseases or long-continued suppurative processes, when one of the more active lesions is not established. But the exact reasons for its development have not been clearly explained.

Pathological Anatomy.—The kidneys are much larger than normal, weighing from five to eight ounces (141.747 to 226.796 grams) or more. Their color is markedly pale, and their capsules are normal and non-adherent to the underlying renal surface, which remains perfectly smooth after they have been removed.

The cut surface is fatty and almost white, the pyramids are indistinct.
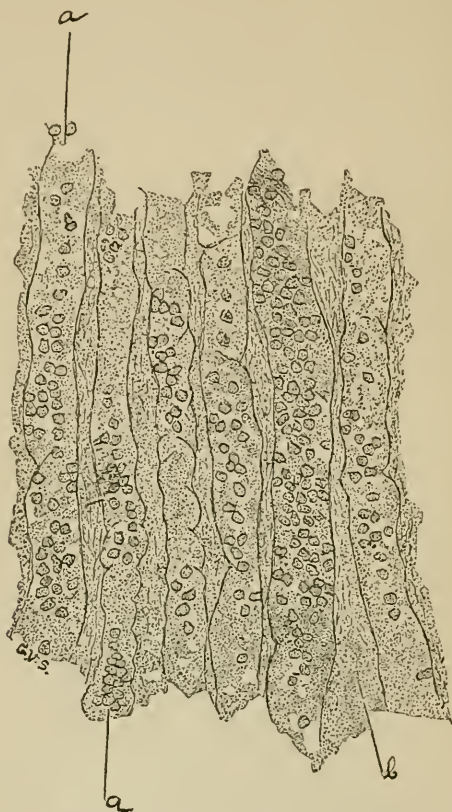
FIG. 13.—CHRONIC PARENCHYMATOUS METAMORPHOSIS OF WASTING DISEASE. × 350.
a, Tubules showing fatty infiltration of the epithelial cells; *b*, œdematous intertubular tissue.

Upon *microscopic examination*, the epithelial cells are found to be swollen and filled with large fat droplets. The cells are seldom separated from the basement-membrane, and consequently the lumen of the tubule remains open. There is little or no change in Bowman's capsule.

In chronic cases, there may be a slight increase in the interstitial tissue, but even this is rare.

Symptoms.—Occasionally slight œdema of the eyelids and of the extremities may be noticed, which would lead us to suspect the existence of some lesion of the kidneys; but further than this, no symptoms except those referable to the inducing disease make their appearance.

The *urinary analysis* is practically negative.

Prognosis and Treatment.—The renal complication of the original disease gives no trouble to the patient and is not to be feared by the physician. The prognosis is, of course, unfavorable, but does not depend upon the lesion of the kidneys, which would disappear should the patient recover from the chronic and primary disease.

This lesion so closely resembles in its gross appearance the other parenchymatous changes, and is so often found at the necropsy table, that it has been deemed best to describe it with the other parenchymatous forms, but it should be remembered that its causation, minute anatomy, and clinical symptoms are absolutely different from the other varieties.

The three lesions just described resemble each other very closely in their macroscopic appearance, but each one has its special anatomical and clinical feature which renders it quite distinctive and by which it can be diagnosticated.

The first and second are practically identical both in their macroscopic and microscopic appearances, but the third differs in its minute changes, and is, more strictly speaking, a functional disease, while the other two are active and destructive lesions.

By having a clear conception of the pathological changes, and by fully comprehending every step in the causation and method of production, their treatment must of necessity be more intelligently directed, enabling us often to anticipate, rather than to wait for symptoms before applying our therapeutic agents.

In their macroscopic anatomy they are almost identical and cannot readily be separated, but the variety associated with wasting diseases is usually the palest of the three and the most fatty; this, however, is not an invariable rule. Microscopically, in the third form the change in the epithelial cells is found to be composed of an infiltration into the protoplasm of well-defined oil droplets; in the other two the protoplasm of the cells has undergone a granular change, and the fat droplets are very minute particles, indicating a more complete destruction of the cell-mass. But by a careful study of the clinical history, they are easily isolated. The first represents the highest type of destruction; the last, the lowest; and that form which is associated with pregnancy holds the intermediate position.

Of the three, the intermediate form is the least fatal, the other two

standing about equal; the first producing death by itself, the last only by the disease which causes its development.

In the first and the second, there is a true metamorphotic change, but the last is passive, and simply imbibes fat droplets without destruction of the renal protoplasm; it is analogous to the fatty liver of similar diseases.

They are all classed in this group because the change is primary and chiefly located in the epithelial cells; and they are not inflammatory in origin, but are due to overwork and impaired nutrition. The last is classed here, not only for convenience, but also and especially from its close external resemblance to the first and the second, and the frequency with which it is met with at the necropsy table. At the same time it should be remembered that the last variety is not an essential lesion, and does not give rise to either rational or clinical symptoms.

ACUTE DIFFUSE NEPHRITIS. CHRONIC DIFFUSE NEPHRITIS, FIRST, SECOND, AND THIRD FORMS.

ACUTE DIFFUSE NEPHRITIS.

Definition.—Acute diffuse nephritis is that variety in which the intertubular tissue is infiltrated with new cells in addition to a parenchymatous metamorphosis of the epithelial elements.

There is now every indication of a true inflammatory condition, for there is a migration of the blood-corpuscles into the intertubular tissue and an exudation of all the constituents of the blood into the renal substance, most of which, however, escape from the glands with the urine.

Etiology.—This lesion is chiefly met with as a sequela of acute diseases, and is especially frequent after scarlatina. It is occasionally developed in connection with severe burns, but it is more frequently produced by sudden and severe exposure to cold; and as the result of irritating diuretics, such as turpentine, cantharides, etc.

A very large percentage of the cases, however, occur as a complication to or as a sequela of scarlet fever, and when we add to this the cases in connection with diphtheria, the disease becomes in its primary origin almost exclusively one of childhood.

The cases following sudden exposure to cold or severe burns, and as an exacerbation to a chronic nephritis, are more frequent in adult life.

Many of the deaths which follow the acute diseases, especially in children, are really due to this complication or sequela, and not to the original disease itself. When this fact is fully appreciated and guarded against, the mortality will decrease.

During the course of an acute disease of any kind, the renal epithelial cells are called upon to perform an unusually large amount of work, and at the same time their nutrition is decidedly impaired. These cells may accomplish this task without a parenchymatous metamorphosis sufficiently advanced to give rise to clinical symptoms, but they are, nevertheless, weakened, and any little exposure or careless-

ness on the part of the patient during convalescence, while the renal
cells are in this impaired condition, may suddenly interrupt the
normal process. An increased amount of work is thus thrown upon
these cells, which, in addition to reproducing the parenchymatous
metamorphosis, also establishes a true or diffuse inflammatory condi-
tion. For these reasons the greatest care should be exercised
in guarding the kidneys against these severe strains during the height
of the attack, and still more so against damage during convalescence.
By remembering these etiological factors, many an acute nephritic

Fig. .14—ACUTE DIFFUSE NEPHRITES. × 350 and reduced.

Case of Scarlatina. *a*, Swollen endothelium of the glomerulus; *b*, proliferation of lining cells
of glomerulus; *c*, compressed vascular tuft; *d*, swollen stroma infiltrated with cells; *e*, dilated
convoluted tubules; *g*, swollen epithelium peeling off; *h*, hyaline cast. (Delafield and Prudden's
"Handbook of Pathological Anatomy and Histology.")

attack may be warded off; and in this way, if in no other, the patient
may be spared a chronic form of the disease later in life.

Pathological Anatomy.—The kidneys are usually very much en-
larged and sometimes weigh ten ounces (283.496 grams). In rare
instances, however, they are not much altered in size. In either
case their capsules are non-adherent to the underlying renal
substance, the surface of which is found to be smooth and dark
after enucleation. The stellar veins of Verheyen are distended
with blood, the cut surfaces are dark in color; the cortex and pyra-

mids of Malpighi are congested and often the seat of ecchymotic
spots. Later in the disease the cortex is pale, and often œdematous,
contrasting strongly with the dark and congested pyramids. The
markings are straight and the Malpighian bodies unusually promi-
nent.

On *microscopic examination,* the epithelial cells are found in the
usual condition of parenchymatous metamorphosis, or granular
transformation of the cell protoplasm, and the intertubular tissue is
swollen, œdematous, and infiltrated with new cells. In the early
stage, the vessels are distended with blood, but later on this conges-
tion is less marked. There is now an apparent increase in the num-
ber of cells, or cell nuclei, covering the Malpighian tuft and lining
Bowman's capsule, which, in severe cases, causes a compression of
the tuft of vessels within the capsule. This infiltration of the Mal-
pighian tuft has been considered diagnostic of the renal lesion
which is a sequela to scarlet fever. This, however, does not hold
true, for the same condition is found where the nephritic lesion
has resulted from other causes. It, perhaps, is more likely to be
present on account of the greater severity of the disease in these
instances.

Small extravasations of blood into the glomeruli are often found.
Numerous leucocytes are found throughout the section, but not in
quantities sufficiently large to simulate a suppurative or pyelo-
nephritic condition. A marked difference can be seen between this
lesion and the parenchymatous metamorphosis which occurs dur-
ing the height of the attack. In the former, all the structures
are implicated, and there is every indication of an inflammatory
condition, while in the latter only the epithelial cells are involved
without any of the lesions common to inflammation, the change
being a granular metamorphosis from overwork and impaired nutri-
tion.

The *symptoms* depend largely upon the cause of the renal lesion,
and naturally vary with them. When the patient is attacked with
acute diffuse nephritis, and the cause is exposure to cold, or perhaps
cannot be discovered, there is usually an initial chill, followed by
fever, pain in the back and region of the bladder, difficult and fre-
quent micturition, and a very much diminished quantity of urine.
Such cases may be divided into groups according to severity.

a. In very acute cases, these symptoms are rapidly followed by
signs of uræmic poisoning, convulsions, coma, and death, which en-
sues in from twenty-four to thirty-six hours.

b. In subacute cases, œdema of the inferior eyelids and feet appears in a day or two after the invasion, followed by general anasarca, while dropsy, abundant or otherwise, may make its appearance. The cephalic symptoms are those of the milder type of renal affections, consisting chiefly of pain in the head, drowsiness, and stupid feelings, but delirium rarely occurs. After a few days or weeks, the symptoms improve, and the patient is apparently cured, although some albumin and a few casts may persist, and be found in the urine for six months or a year.

c. In still other cases of a milder type, œdema and dropsy are the first symptoms that present themselves. There may be some nausea, slight pain in the back and in the region of the bladder, and dimness of vision. These symptoms are followed after a short time by a waxy pallor and a very anæmic condition, the nausea giving place to violent and often persistent vomiting. The patient is much bloated from the anasarca and dropsy, and may become " water-logged." Drowsiness and stupor are often quite marked. In these cases, the sight may be impaired from a retinitis, or inflammation of the optic nerve, but more frequently from an imperfect nutritive condition of the optic centres, or what is known as a central lesion. These symptoms, however, gradually disappear, although, as in the former class, the albumin and casts persist in the urine for a considerable time.

d. When the acute diffuse nephritis appears as a sequela to scarlet fever, it usually develops on the fourteenth, the twentieth, the twenty-first, or the twenty-second day; that is, from the second or third week after the invasion. This is the time when desquamation is most active, the skin very sensitive, and the patients restless from confinement. They slip from a warm to a cold room, or a window is left open, and the child is exposed to a sudden and cold current of air. In this way, almost unnoticed, the surface is unexpectedly chilled, the physiological processes at once interrupted, more work precipitated upon the already weakened kidneys, and the nephritis set in motion, suddenly, and apparently without cause, the increased temperature returns; headache, drowsiness, and stupor make their appearance, and the diagnostic waxy pallor of nephritic disease is developed. There is myalgia, œdema of the face and extremities, followed shortly by general and extensive anasarca, abundant dropsy of the large cavities, and great dyspnœa. In the worst cases the urine is suppressed, and convulsions, coma, and death rapidly ensue.

The *urinary symptoms* in all the above-described varieties are similar; they are always present, but vary somewhat with the severity of the attack. The following is a synopsis of these symptoms in a typical

case of acute diffuse nephritis. The urine is diminished in quantity, sometimes suppressed, and dark, smoky or bloody in color, and albumin is abundant. The specific gravity, although the quantity of urine passed is small, instead of being high as is the case in the acute parenchymatous form, ranges usually between 1.020 and 1.012.

Upon microscopic examination, it is found to contain red blood-corpuscles, leucocytes, and epithelial cells; blood casts, small hyaline, nucleated, epithelial, and finely granular casts, with a considerable quantity of granular *débris*.

The large amount of blood-corpuscles, and the presence of a large number of blood-casts, are the positive and diagnostic features of this lesion. During recovery, the specific gravity of the urine may rise above normal, and the albumin gradually diminish in quantity.

Diagnosis.—The only lesion with which it could be confounded is the acute parenchymatous metamorphosis, but from which it is easily differentiated when we remember that the parenchymatous lesion occurs during the attack, while the diffuse nephritis occurs as a sequela. The urine of the parenchymatous variety does not contain blood or blood-casts, but they are abundant in the acute diffuse nephritis, and it is the blood and blood-casts which stamp this lesion, and which are the differential characteristics.

The *prognosis* depends entirely upon the severity of the renal disease, as well as the severity of the original attack, also upon a careful study of the symptoms, an early recognition of the disease, and a judicious method of treatment. If the attack be mild in its onset, and the treatment be well directed, the prognosis is favorable; otherwise the reverse will prove true. A very severe case at the onset, if properly handled, may be subdued, and ultimately made to terminate in recovery.

Those forms of disease which do not occur as a sequela, or complication of scarlet fever, or some of the other acute disorders, are apt to become chronic, and eventually to prove fatal. Quite a number of the mild cases rightly treated will recover. With a clear understanding of the methods of production, and a treatment based upon it, an improved prognosis will result.

The *treatment* naturally falls into three headings, the preventive, the management of the acute invasion, and that of the more chronic stage. Under prevention, all that tends to ward off the development of an acute parenchymatous metamorphosis should be vigorously enforced. The skin and bowels should be kept acting freely, thus relieving the strain upon the kidneys. Cold applications to the skin

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should be avoided. Non-irritating diuretics should be freely admin-
istered, and the saline diuretics avoided.

During the invasion, when there is renal congestion and threatened
suppression of urine, dry cups applied to the loins, and frequently
repeated, will be found of service, or wet cups, not repeated, are often
very efficacious. Or hydrargyri chloridum mite, gr. ij. (0.1
gram), with opium gr. $\frac{1}{2}$ (0.03 gram), may be given every two
hours, followed by castor oil. This plan of treatment is specially
indicated when the bowels are constipated. Jalap and calomel, five
to ten grains (0.3 to 0.6 gram) each, will be found of service.
Elaterium, however, in small and repeated doses, has been found
the most efficacious remedy in uræmic conditions, as it appears to re-
move from the system the uræmic poison more rapidly and effectually
than any other eliminating agent. It produces free and copious
watery discharges; keeps down the œdema; greatly relieves the strain
upon the kidneys; renders the patient quite comfortable, and is a
great aid in effecting a cure. Jaborandi, or its alkaloid pilocarpine,
may be used; if the latter, it is best employed hypodermatically, but
by some it is considered dangerous in this condition, on account of the
shock which it is supposed to give to the system. From observing its
action in large doses and in quite a large number of cases, only one
deduction is possible: that it is not depressing to any noticeable
degree, and is always followed by the most desirable results, both to
the physician and to the patient. Recorded observations, however,
are quite contradictory on this point, and its action should be care-
fully watched. Spiritus ætheris nitrosi, digitalis and its preparations
may be used for their diuretic and diaphoretic properties; also large
draughts of water, demulcent drinks, and some of the mineral waters.
Hot-air baths at times may be used, and are often serviceable.

Digitalis and its preparations are the only safe remedies during this
acute stage. They are non-irritating diuretics, and act principally by
contracting the arterioles, and increasing the general blood pressure;
in this way increasing the pressure upon the glomeruli. They probably
have less effect upon the tension of the renal arterioles than on the rest
of the circulatory system, otherwise they would diminish instead of
increase the flow of urine. Further investigation will probably show
that digitalis only acts when there is a venous congestion of the inter-
tubular plexus of veins. Some have advanced the idea that this drug
has a specific and unexplained action directly upon the kidneys,
especially upon the Malpighian tuft. The increased general blood
pressure and the condition of the intertubular plexus explains the so-
called specific effect.

The potassium salts, here as in acute parenchymatous metamorphosis of the kidney, are contra-indicated, page 25.

Opiates, whether admissible in adults or not, are decidedly contra-indicated in uræmic attacks in children.

After the acuteness of the attack has passed off, and it tends to assume the chronic form, the tinctura ferri chloridi in full doses will be found a most reliable remedy.

The food should be of the best ; plain, easily digested, nutritious, non-irritating, and such as will yield the least amount of effete material. A simple milk or skim-milk diet often proves most satisfactory.

During the convalescence, great care should be exercised in keeping the bowels active. One free movement daily should be the rule. The skin also should be kept active by sponging and friction. All exposure to sudden changes in temperature and excesses in diet should be scrupulously avoided. By a strict observance of the above rules, the work to be performed by the kidneys is reduced to the minimum, while their nutrition is increased to the maximum, and many cases are caused to terminate in a complete recovery, which otherwise would run into a chronic form of renal disease, and result in an untimely death.

In this lesion, the plan of treatment detailed on pages 25 and 26 will be found to give the most satisfactory results.

Chronic Diffuse Nephritis.

Introductory Remarks.—In this group of renal lesions, all the structures of the kidneys are involved. The epithelial cells undergo a parenchymatous metamorphosis, and the intertubular tissue a cellular infiltration and thickening. There are three distinct varieties: in one the kidneys grow large from the major part of the lesion being located in the epithelium; in the other two, the organs are diminished in size, in one with, and in the other without, a hyaline thickening and expansion of the afferent vessel of the Malpighian coil.

Chronic Diffuse Nephritis.

FIRST VARIETY: FOURTH FORM OF LARGE WHITE KIDNEY.

Definition.—Chronic diffuse nephritis is an inflammation which involves the interstitial tissue of the kidneys, associated with a chronic parenchymatous metamorphosis of the epithelial cells lining the uriniferous tubules, but which differs from the acute variety in its duration, and in the extent of interstitial involvement. In this peculiar variety, the disease spends its greatest force upon the paren-

chyma. It assumes somewhat the type known as chronic parenchy-
matous metamorphosis, but it has added to that, the interstitial diffi-
culty which now is of an inflammatory nature and not simply an
œdematous thickening.

Etiology.—The exact cause and method of production in the
chronic diffuse class cannot be so perfectly traced as in the parenchy-
matous group and in the acute diffuse variety. From its infrequency
in the tropical and frigid, and its great frequency in the temperate
zones, its cause is probably dependent upon the repeated exposure of
the surface of the body to sudden and alternating influences of
heat and cold, which have a tendency to produce recurring attacks of
internal congestion and overwork on the part of the kidneys, until
finally this condition is fully established.

Its frequency among bakers, foundrymen, and engineers points in
this direction. Some have ascribed rheumatism as a cause, but the
climatic influences which excite the rheumatism appear to be the
chief exciting causes of the renal lesion.

It certainly is common among brain workers who take but little
exercise and at the same time live rather highly. In some instances
it unquestionably follows an acute attack. Very frequently it is de-
veloped without any well-defined cause being ascertained. Repeated
attacks of pneumonia, fevers in general, and all severe diseases which
tend to overwork the kidneys are very potent causes for laying the
foundation of and paving the way for this variety of renal lesion.

Pathological Anatomy.—The kidneys are pale in color and may be
normal or slightly diminished in size, but *as a rule* they are markedly
enlarged. Their capsules are thickened and slightly adherent, and,
upon removal, often bring with them small portions of the underlying
renal tissue, but between the adherent spots the surface of the glands
may be quite smooth, or only slightly granular.

The exterior and cut surfaces show numerous small cysts, with here
and there a large one. The cortical layer is usually increased in
thickness and pale in color, and its markings are wavy, while the
pyramids are less prominent than normal.

Microscopic Examination.—The interstitial tissue is seen to be
moderately increased in quantity, and the seat of small round inflam-
matory corpuscles. Bowman's capsule is thickened by an inflamma-
tory exudation, and the epithelial cells are found in a state of fatty
and granular disintegration. The blood-vessels are but little, if at all
affected. The only difference between this lesion and that known as
chronic parenchymatous metamorphosis, is the marked evidence of an
inflammatory exudation and thickening in the interstitial tissue. In

this variety, the major part of the lesion is parenchymatous in character, with only a moderate amount of interstitial involvement, and consequently the kidneys tend to progressively enlarge throughout the course of the disease.

Symptoms.—In those cases which occur without known cause, the symptoms are very insidious: convulsions and coma rapidly followed by death may be the first indication; but more frequently its onset is marked by frontal headache, impaired vision, nausea, vomiting, dyspepsia, shortness of breath, weakness, general malaise, œdema, and after a time, a peculiar waxy pallor of the skin, and dropsy or general anasarca.

In some cases, a persistent diarrhœa, either alone or alternating
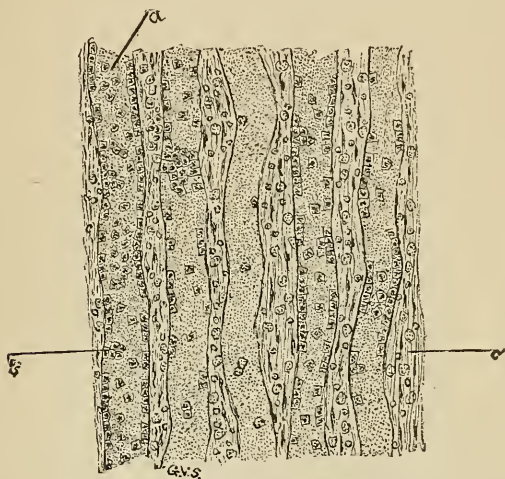
FIG. 15.—CHRONIC DIFFUSE NEPHRITIS. × 350.

a, Uriniferous tubule showing marked metamorphotic changes in the epithelium; *b*, desquamating epithelium; *c*, new-formed intertubular tissue.

with periods of obstinate constipation, is a marked symptom. The stomach and intestinal symptoms may be present together or may alternate with each other. The amount of œdema and dropsy varies in the different cases from a slight puffiness under the eyes to a great distention of the skin, and a filling of the large serous cavities with effused fluid; this symptom is almost always present and frequently to a marked degree.

The dimness of vision may be due to interference with the cerebral nutrition without any perceptible lesion of the visual apparatus; it may be due to simple neuro-retinitis, to neuro-retinitis accompanied by a degeneration of the nerve elements, to the formation of

connective-tissue patches in the retina, to emboli, or to apoplexy of the retina. Where any of these lesions occur, there will be no interference with the sense of sight, so long as the macula lutea is not encroached upon. The lesions of the retina are generally symmetrical, and occur near the outer side of the optic nerve, appearing first in white spots of small size, and of a quadrilateral shape, which coalesce as they progress, and finally involve the optic disc. Extravasations of blood from rupture of the retinal vessels are occasionally seen, and the disc and the retina in its immediate neighborhood have a striated appearance. Later on, the fundus becomes quite yellow, owing to a hyperæmia followed by an œdematous infiltration of the retinal tissue, which finally causes a fatty degeneration of its substance, a giving way of the blood-vessels and hemorrhagic extravasations.

Urinary Symptoms.—The quantity of urine voided varies greatly; at times, it is much less than normal, at others more abundant, or it may be suppressed for several hours. This continued fluctuation in the quantity is one of the chief diagnostic points. Its color is, as a rule, pale. The urine in this group of chronic nephritic lesions has as a characteristic feature a diminution or complete absence of perceptible sedimentary deposits, and for this reason casts are often overlooked, or thought not to exist, but a careful study of the lower strata of fluid under the microscope will usually reveal their presence. Neglect of this has often caused a mistake in diagnosis. The specific gravity ranges from 1.025 to 1.012, and may fall as low as 1.005. It is most frequently found to be between 1.017 and 1.010. Albumin, although varying in quantity, is usually present during the whole course of the disease, but it may disappear for days or even weeks, while the casts will be constantly present. Both, however, may disappear for a time, or the casts may disappear, and the albumin persist. The rule, however, is to find a fair amount of albumin nearly all the time.

The casts most commonly found are the hyaline, coarsely granular, and fatty, which are generally of large or medium size.

In acute exacerbations of the disease, all forms and sizes of casts and some blood may be present. Such attacks are frequently mistaken for an acute and primary diffuse nephritis.

Prognosis.—Patients with this disease seldom entirely recover, but they may live ten, fifteen, or more years without much discomfort. There is, however, more or less drain upon the system, which renders the prognosis of any acute disease which they may contract particularly unfavorable. There is little doubt that the existence of an

insidious form of this lesion is one of the chief causes for the frequent fatal termination in cases of pneumonia. It also suggests the necessity for *a closer investigation into the true condition of the kidneys in all acute diseases.* An acute exacerbation is likely to occur at any time, and always renders the prognosis bad.

Treatment.—As our knowledge of the causes of this lesion is somewhat obscure, as compared with the parenchymatous group and the acute diffuse form, much less can be accomplished in the way of preventive treatment. All excesses should be avoided. As climate is ascribed as a cause of the malady, the body should be well protected by flannels, so that sudden changes will produce the least impression upon the system.

The treatment of this and the two following varieties being nearly the same, the three will be spoken of together.

CHRONIC DIFFUSE NEPHRITIS.

SECOND VARIETY: SECOND FORM OF SMALL KIDNEY.

In this, the second variety of chronic diffuse nephritis, the disease spends its force upon the epithelial cells, the interstitial tissue, the arterioles, and the capillary blood-vessels. The greatest intensity of action is located in the intertubular tissue and afferent vessels. There is a marked production of new interstitial tissue, and the small arterioles undergo a hyaline transformation which causes a thickening of their walls and an increase of the lumen.

The change in the epithelial cells does not compare in extent with that in the intertubular tissue, nor is it as great as that which occurs in the first variety of chronic diffuse nephritis or the chronic parenchymatous form. There are, however, some primary metamorphotic changes in the epithelial cells, which prevent this lesion from being classed as a sclerotic kidney.

Etiology.—The cause for this particular form has not been absolutely determined.

The same causes which produce the former lesions appear to act in like manner in this one.

Believing the peculiar hyaline change met with in the vessels in this form to be diagnostic of a systemic syphilitic taint, and from the fact that a specific history was obtained in most of the cases in which this peculiar lesion was present, the most natural inference is that the syphilitic poison is a factor in determining the character of the lesion.

In this form of atrophic kidney, we find a similar hyaline change in the small arterioles throughout the body, and usually an hypertrophied

heart, but in the next form the vessels are not implicated, and the atrophic heart is the rule. Hence it appears that the cardiac hypertrophy is due to the general loss of arterial elasticity, and is in no way directly dependent upon the renal circulation, or vice versa.

The retinal lesions so frequent with this variety and the sclerotic forms, in which there is also a general vascular change, are, like the hypertrophy of the heart, dependent upon the impaired condition of the blood-vessels throughout the body, and not to either the renal or cardiac condition alone. The tension upon the circulation is constantly fluctuating, and, at the same time, the nutrition of the vascular walls are impaired, and they soon give way under the unequal strain produced by the cardiac hypertrophy, the loss of arterial elasticity, and the imperfect elimination by the kidneys.

Fig. 16.—Section from Cortical Portion Showing Thickened and Expanded Afferent Vessel. × 350.

Pathological Anatomy.—The kidneys are diminished in size; their capsules are thickened and very firmly adherent to the underlying surface. The renal tissue is pale and finely granular upon the exterior. They are small white and granular kidneys. Small cysts are often present. The cut surface shows the cortex to be thinner than normal, and if enough remains, the markings will be wavy. The pyramids are also diminished in size.

The microscopic examination shows a great increase in the interstitial tissue, and tortuosity of the normally straight or collecting uriniferous tubules. In these tortuous tubes, twisted casts are occasionally seen in the sections, and, if discharged with the urine, as frequently they are, they appear in the urinary examination as the corkscrew casts. The new tissue is studded with small round inflammatory corpuscles. Bowman's capsule also shows evidences of a true

inflammatory thickening, due to the production of new tissue. By the contraction of this newly formed tissue, the tuft of vessels within the capsule is often compressed. In this particular form of lesion, there is a marked thickening of the small arteries and afferent vessels of the Malpighian tufts. This peculiar hyaline transformation causes a thickening of the arterial wall and a permanent increase in the lumen of the vessels.

There is an advanced stage of granular and fatty metamorphosis of the epithelial cells, but the change does not appear to be one due to atrophy from compression, as in the sclerotic kidney, but to intrinsic changes in the epithelial protoplasm. This positive change in the cell elements is essential to render the lesion diffuse.

Many of the tubes are found entirely stripped of their epithelial lining, and the remaining basement membrane collapsed and converted into fibrous cords, which appear under the microscope as bands of fibrillated connective tissue.

The occlusion of the tubes in this manner is one of the ways in which the cysts, so frequently seen upon the surface, are formed. The surface of these kidneys may have numerous cicatricial depressions, which have been developed by the collapse of one of these cysts, or resulted from the absorption of an infarction.

The latter mode of formation is the more frequent, but has no special bearing, as they are found in many other varieties and in otherwise normal kidneys.

Symptoms.—The general symptoms are the same as those of the first variety, the only marked point of difference being in connection with the urine, which is here very much increased in quantity, the daily amount varying between seventy-five and one hundred and fifty ounces.

This large increase is explained principally by the thickening of the walls of the arterioles. They lose their power of regulating the tension brought to bear upon the capillaries of the glomeruli. There is no longer any method by which the pressure can be equalized and the full and irregular pressure of the circulation is brought to bear directly upon the tuft and, therefore, the water passes rapidly through the walls of the vessels into the tubules. The involvement of the epithelium and the compression of the intertubular plexuses are the causes of the large amount of albumin present in the urine. This assertion is sustained by the pathological fact that in all cases in which the epithelial cells are primarily involved, with compression of the intertubular vessels, albumin is always present in large quantities.

The extent to which these two anatomical portions are involved

determine quite positively the amount of albumin discharged. The assertion that the increase in the quantity of water is due to the condition of the arterioles and capillaries is warranted by an abundance of clinical and pathological data. In this, as well as in the sclerotic and amyloid varieties, where there is a marked thickening of the walls of the vessels, the quantity of water discharged is always very large.

In all renal lesions, where the change is primarily in the epithelial cells, with compression of the intertubular capillaries, the arterioles not being involved, the urine is normal or diminished in quantity and the albumin abundant. On the other hand, if no change occurs in the epithelial cells, albumin is absent.

Prognosis.—The duration of the disease is very uncertain. From a pathological standpoint, involving, as it does, all the structures, it would be short ; but clinically it borders more upon the sclerotic type; and the prognosis is quite as favorable, if not more so, than the first form.

Treatment.—The treatment of the different varieties of diffuse nephritis will be spoken of together later on.

CHRONIC DIFFUSE NEPHRITIS.

THIRD VARIETY: THIRD FORM OF SMALL WHITE KIDNEY.

Definition.—This variety of chronic diffuse nephritis differs from the other two in that both the interstitial tissue and the epithelial cells are about equally involved, while the glands progressively diminish in size. In this variety, there is comparatively little development of new connective tissue, but it is given a greater prominence owing to the rapid atrophy of the epithelial elements. There is no increased thickening of the arterial walls.

Etiology.—The causes, so far as known, are similar to those in the two former lesions. Previous attacks of acute disease may have unduly damaged the renal epithelium. The form of the chronic lesion, whether parenchymatous or diffuse, is as a rule determined by the form and severity of the acute attacks in the past; that anatomical portion of the kidney tissue which suffers the greatest damage during the acute attacks being the portion where the chronic form becomes seated. In this way the different varieties can be accounted for, just as in a machine the part receiving the greatest strain will be the first to give way.

Pathological Anatomy.—The kidneys are very small, and their cap-

sules are thickened and firmly adherent to the underlying renal tissue, which is very pale, fatty, and granular. Cysts are frequently present upon the surface. The cut surfaces show the cortex to be thin and often almost obliterated. If there is enough left to judge from, the markings are wavy. The pyramids are always pale and atrophied. In macroscopic appearance, they might easily be mistaken for the sclerotic variety, but both the external and cut surfaces are paler than normal. This is the small soft kidney.

Microscopic examination shows an increase in the amount of intertubular tissue, which is partly due to a new-formation of connective

FIG. 17.—CHRONIC DIFFUSE NEPHRITIS. ATROPHIED KIDNEY, × 350 and reduced.

Showing small patches of new connective tissue with atrophy of inclosed tubules. *a*, new connective tissue; *b*, atrophied tubule containing hyaline casts; *c*, tube with epithelium peeling off; *d*, thickened capsule of glomerulus. (Delafield and Prudden's "Handbook of Pathological Anatomy and Histology.")

tissue, and partly to the rapid destruction and desquamation of the epithelial elements, with a collapse of the basement tube. Bowman's capsule is thickened by as light amount of newly formed connective tissue, which in some instances, owing to the general shrinkage of the organs, causes compression and collapse of the tuft, followed by atrophy. There is, however, in this variety no involvement of the arterial capillaries, and in this respect it differs from the former lesion.

The epithelial corpuscles are extensively involved by a destructive metamorphosis which is both granular and fatty. This extensive destruction of the epithelial cells, and the contraction of the newly formed tissue, account for both the softness and the great diminution in the size of the gland.

This form of lesion probably produces the smallest variety of kidney, and one which is soft instead of hard, distinguishing it from the previous form and the sclerotic and gouty varieties. In one instance, one kidney weighed one and a half ounces (42.524 grams), and the other only one ounce (28.349 grams).

Symptoms.—The general or rational symptoms are about the same as in the other forms of chronic diffuse nephritis. There is usually considerable dropsy.

Diagnosis.—The changes in the urine are the means by which a correct diagnosis is made. The amount of urine voided ranges from fifteen to forty ounces per day, and has the peculiar translucency common to all forms of chronic diffuse nephritis. It is acid in reaction, and its specific gravity ranges from 1.010 to 1.025, usually being high. In this respect, it resembles a purely parenchymatous lesion, but its color is pale, while the parenchymatous group, as a rule, yield a high-colored urine.

Albumin is constant and abundant; this is also true of the parenchymatous group. In this lesion, all forms of casts are found, and they vary greatly in size; but in the chronic parenchymatous, the large hyaline, coarsely granular, and fatty casts and considerable cast *débris*, are the distinguishing features. Blood casts may occur in this form, but never in the purely parenchymatous group.

From the first form of chronic diffuse nephritis it is distinguished by the small quantity and the continued abundance of albumin and casts, and the high specific gravity.

In the first form, the quantity of urine, the albumin, and casts are constantly fluctuating, while the specific gravity is, as a rule, abnormally low.

In the second form, the quantity of urine and the amount of albumin are always large, ranging from sixty to one hundred and twenty ounces per day, casts of the small hyaline and fatty varieties being the only kind found, and these in small numbers. The urine also has a specific gravity rarely above 1.010.

Prognosis.—This is undoubtedly the most fatal form of the diffuse group, after the symptoms become pronounced. The prognosis does not date from the starting-point of the disease, but, in the majority of instances, from the time when the symptoms become sufficiently

marked to attract the patient's attention and cause him to consult a physician.

In some, if not in most, of the cases, it is impossible to say when the disease first commenced, and how long it had existed when first diagnosticated. Many cases undoubtedly exist for a long time, without attracting the attention of either patient or physician. But a more frequent microscopic study of the urine would unquestionably reveal the lesion much earlier.

Usually, the disease creeps along in its insidious course until some indiscretion, excess, or overstrain on the part of the individual throws an extra amount of work upon the kidneys, the epithelial cells are damaged beyond toleration, troublesome symptoms declare themselves; the patient's attention is attracted to these acute manifestations, and a physician is consulted, who at once recognizes the difficulty.

COMPLICATIONS OF RENAL LESIONS. TREATMENT OF
CHRONIC DIFFUSE VARIETY.

COMPLICATIONS.

There are a number of conditions associated with the various renal
lesions, that are produced directly or indirectly by the kidney disease.
There are also other conditions which are concomitant lesions, but
which unquestionably act as complications. Some of the symptoms,
as they become more aggravated, are classed as such; and for conveni-
ence all of them will be considered as complications, and, taken up in
alphabetical order, and not with reference to their frequency or im-
portance.

(*a.*) *Ascites, Hydroperitoneum, or Abdominal Dropsy.*—This con-
dition is a part of the general dropsy, instead of a new and complicating
disease, and usually, if moderate in extent, causes little inconve-
nience; but when excessive, it crowds up the diaphragm, materially
interfering with the respiratory movements, causing dyspnœa, and
often increasing the immediate danger. An associated portal
obstruction may also aid or produce ascites, and in this way complicate
the renal lesion.

Treatment.—Unless the abdominal dropsy becomes excessive, it will
not necessitate paracentesis abdominis. The ordinary methods for
treating the general dropsy with the free use of hydragogue cathartics
will generally remove the trouble without an operation.

(*b.*) *Aneurisms.*—The variety here referred to is that commonly
known as Charcot's, or the miliary aneurism. These are quite com-
mon in the cerebral substance, and have also been observed in the
small intestine, stomach, and in the pulmonary tissue.

By their rupture, both in the stomach and intestine, a fatal termi-
nation has resulted from internal hemorrhage, but this is more fre-
quently the case in the brain. In this way many of the cases of
sudden death, without pronounced uræmic symptoms, are explained.

The impaired condition of the small vessels is probably brought

about by the deteriorated condition of the blood, which diminishes the nutritive supply. This form of aneurism is most frequently met with in connection with those cases in which there is high or increased arterial tension and left cardiac hypertrophy, or in connection with the second form of chronic diffuse nephritis and the sclerotic or interstitial variety.

Their rupture is considered by some to be the only cause of cerebral hemorrhage, not only in connection with nephritic disease, but in every instance.

Four cases will be cited, illustrating this point. In each, death was rather sudden and unexpected, associated with all the ordinary
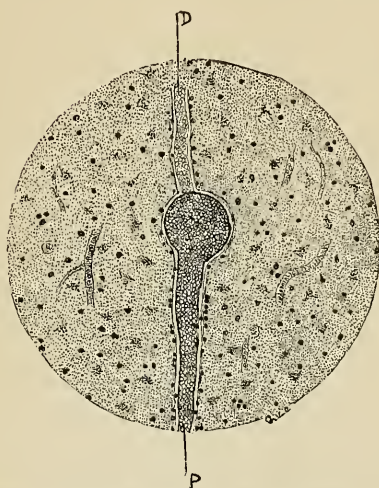
FIG. 18.—MILIARY ANEURISM IN THE CORTICAL SUBSTANCE OF THE BRAIN DIVIDED LONGITUDINALLY.

p, Proximal side of vessel, its diameter being 1/54 of an inch; *d*, distal end of vessel its diameter being 1/128 of an inch. The greatest diameter of the aneurism being 1/20 of an inch, its smallest diameter 1/29 of an inch.

signs and symptoms of internal hemorrhage, and without any symptom of a uræmic nature. In two of the cases, the aneurism was located in the wall of the stomach and the hemorrhage poured into its cavity. The history of one of these cases was as follows. The patient was admitted to the hospital for a severe hæmatemesis. The blood vomited was abundant and arterial in character, some was also passed through the anus. Physical examination of the chest gave a negative result. The urine contained albumin and casts, establishing the existence of a renal lesion. Death soon occurred with all the ordinary symptoms common to internal hemorrhages.

The diagnosis is made by excluding all the other causes for hæmatemesis, viz., ulcer of the stomach, sclerosis of the liver, and all forms of portal obstruction, cancer or toxic inflammations of the stomach, pernicious anæmia, leucocythæmia, purpura hemorrhagica, scurvy or scorbutus, yellow or typhus fever, jaundice, acute atrophy of the liver, pyæmia, pulmonary or cardiac lesions, vicarious menstruation, and the bursting of an extrinsic aneurism into the œsophagus or stomach.

With the rupture of a miliary aneurism in the stomach, the hemorrhage comes on without premonitory symptoms, aside from those of renal disease; it is abundant and rapidly fatal. Microscopic examination revealed the same condition as represented, Fig. 18, page 63, but the vessel implicated was much larger and, having ruptured, its outlines were not as perfect.

In the other two, the aneurism was located in the intestinal tunic. In both there had been a copious hemorrhage into the intestinal canal; while in one of them the blood had also found its way into the peritoneal cavity. Many similar cases have been noticed, until this lesion has become one of the recognized causes of death in the chronic forms of renal disease.

As there are no positive signs by which aneurisms of this description can be recognized until they rupture, they are chiefly of pathological importance in accounting for some of the sudden deaths.

The ordinary aneurism, in connection with the large vessels, may act as a complication; but it is not dependent in any way upon the renal lesions for its production, and when it does occur, it is a coincident disorder. They may cause troublesome symptoms by their pressure, or sudden death by being ruptured.

The rupture of a miliary aneurism is usually followed by a fatal issue, and consequently requires no treatment. The pressure effects of the large aneurism may need attention, and must be treated upon the general principles laid down for such conditions.

(c.) *Apoplexy or Cerebral Hemorrhage.*—This condition is a frequent and fatal complication. It is superinduced in part by the renal lesion causing changes in the blood, which in turn damage the cerebral vessels, and in part by an associated cardiac hypertrophy.

Hypertrophy of the left ventricular wall and the miliary aneurisms already mentioned easily account for the hemorrhage, or the aneurisms alone may be a sufficient cause.

Little can be done in the way of treatment for an apoplectic attack.

(d.) *Atheroma of the Vessels in General, or Endarteritis.*—This

condition is frequently spoken of in connection with renal lesions; in some cases it is very pronounced, while in others it is altogether absent. From these facts this condition might justly be looked upon as a concomitant lesion, and not necessarily as a complication. Some, however, hold that there is always hypertrophy or interstitial thickening of the middle coat, especially of the smaller arteries. Repeated examinations of the vessels in connection with renal disease leads to an opposite conclusion, viz., that the one is not directly dependent upon the other. Occasionally the two may be associated, but not as a rule.

This condition is not often recognized until the necropsy, and consequently is not treated. Should it be diagnosticated prior to death, it can only be treated in a general way.

(e.) *Asthmatic Attacks, Dyspnoea, or Uræmic Asthma.*—Extreme dyspnoea, or attacks strongly resembling those of asthma, are by no means infrequent in chronic nephritis. These symptoms are most marked during the night, but with the approach of morning the bronchial tubes become moistened by an increased secretion of mucus, and the breathing is easier. During the day the patients remain fairly comfortable, but with the return of night the dyspnoea is renewed and the difficulty in breathing often becomes so severe that the patient is prevented from lying down or getting any continuous sleep. This particular symptom is one of the most aggravating to the patient, and exceedingly troublesome for the physician to overcome. It is due to some portion of the retained and incomplete products of tissue metamorphosis acting upon the nervous mechanism distributed to the lungs. The anæmic condition, by diminishing the power of the blood to seize upon oxygen and distribute it to the system, also aids in keeping up the dyspnoea. Abdominal dropsy and pleuritic effusion also aid by diminishing the chest space and impeding the respiratory movements. The principal cause, however, is the retained effete products which keep up the nervous irritation.

Treatment.—This complication is one of the most difficult to overcome. Temporary relief will almost always follow a full dose of the muriate of pilocarpine (gr. ¾) (0.04 gram) hypodermatically. With small and repeated doses, the same effect is occasionally accomplished. By giving a full dose of elaterium, or elaterin, the dyspnoea and asthmatic spasm is often relieved and kept in subjection. It is a good plan to alternate these remedies. Some cases are relieved by full doses of the fluid extract of quebracho. But it must be remembered that none of these remedies have a specific effect upon the causation of the asthma, they merely enable the system to relieve

5

itself temporarily of the excitant. This constant drain would naturally be thought to hasten the fatal issue, but on the contrary it prolongs life and renders it far more tolerable. It appears to sweep away large quantities of water, which carry with it the poisonous elements that are so damaging to the system and constantly keep up the annoying symptoms. The water can easily be replaced, but the other elements are too frequently retained.

If the effete and poisonous substances are retained and allowed to accumulate in the system, they are liable to suddenly produce a fatal termination.

At this point it may be well to say that elaterium has in every instance proved the most efficacious cathartic in renal lesions. In some of the cases from which these conclusions have been deduced, this drug was administered daily for several weeks in succession, and in one case from one-half to three-quarters of a grain was administered daily. The method of giving was in pill form (gr. $\frac{1}{8}$) (0.008 gram) every fifteen minutes until the bowels commenced to move, or $\frac{3}{4}$ of a grain (0.04 gram) had been taken. The continued use in this way did not produce any intestinal irritation during life, and at the necropsy the mucous membrane of the intestine was found to be quite normal, so far as any deleterious action of the drug was concerned.

Many other medicinal agents could be mentioned, but these two are the most certain in giving relief, and have always proved perfectly safe, but often have to be used continuously in extreme cases. All forms of anti-spasmodics are absolutely useless.

(*f.*) *Blood Changes. Hydroœmia.*—The chemical composition of the blood is changed. The specific gravity, corpuscles, and albumins are diminished, but the water is increased in quantity. In some cases, there is an actual increase in the number of the white corpuscles, while the red blood-discs become œdematous and flabby. The urea in the blood is slightly increased. This condition can only be treated by tonics, chalybeates, good food and fresh air; if the renal condition can be improved, the quality of the blood will also improve.

(*g.*) *Bronchitis.*—The acute form may be developed at any time, run its regular course and terminate favorably, or else become established and chronic in nature; but more frequently it commences as a subacute or chronic affection. As both the acute and, especially, the chronic form of bronchial inflammation, as well as the renal lesions, are common in advancing years, they may be called associated diseases; the bronchitis not necessarily depending upon the renal lesion as a cause, but at the same time acting as a complication and rendering the prognosis less favorable. With this

conception, the bronchitis calls for independent treatment, although the condition of the renal organs should not be lost sight of or neglected. The improvement of the bronchitis will often be followed by an improvement in the kidney disease.

Treatment.—Undue exposure to cold should be guarded against as a preventive measure, but, when developed, warmth, with tonic expectorants, will do the most good. The following will be found to speedily relieve these bronchial affections:

℞ Tincturæ Opii Deodorati.................................. ʒ i.
    Ammoniæ Carbonatis et
    Ammoniæ Hydrochloratis..........................āā ʒ iij.
    Tincturæ Cubebæ.................................... ʒ iv.
    Syrupi Pruni Virginianæ ....q.s. ad ℥ iij.
M. Sig. ʒ i. every three hours in water.

(*h.*) *Cardiac Lesions.*—Four sets of morbid changes may be found at the necropsy. (*a*) *Hypertrophy without valvular lesion* (simple hypertrophy). (*b*) *Valvular disease,* wholly independent of, and originating prior to, the renal disorder. (*c*) *An endocarditis* may be excited by the kidney disease, and be followed by changes in the valves, causing either a stenosis or insufficiency of the valvular orifices. (*d*) *Atrophy and softening.*

(*a*) Simple hypertrophy, and especially that form which is limited to the left ventricle, has caused much discussion *pro et con.;* some believing that it is produced by the renal lesion, the change in the blood and blood-vessels, increased tension, etc.; while others argue that the cardiac lesion is primary, while the kidney lesion is secondary to, and caused by, it.

In looking over a large number of necropsy records, this fact was noted, that in connection with the parenchymatous group, and in those forms of chronic diffuse nephritis in which there was no general vascular change, the heart was normal or atrophied as in all wasting diseases. But in that variety of chronic diffuse nephritis in which there was a marked thickening and loss of elasticity in the renal and general arterial system, and in the interstitial variety, with a similar vascular change, there was almost invariably a compensatory hypertrophy of the left ventricle to overcome the general vascular resistance. As only one-third of the renal lesions classed as Bright's are associated with cardiac hypertrophy, it seems reasonable to look for the cause outside of the disturbed renal circulation. In this general vascular thickening and loss of elasticity is found a more potent cause. In

some cases of chronic diffuse nephritis in which the non-eliminating function of the kidneys has come on slowly, and there has been a long-continued blood poison and mal-nutrition, the vascular walls throughout the system become thickened and non-elastic and cause cardiac hypertrophy. But as Bamberger says: " It is not possible to suppose that destruction or obstruction to the current of blood in a few little vessels in the kidney could produce cardiac hypertrophy, or *vice versa.*"

On the other hand, there are marked changes in the blood which produce hydroæmia, diminished nutrition, and a consequent loss of elasticity on the part of the arterial coats throughout the body, which, together with the nervous irritability and the varying arterial tension, so impede the free onward flow of blood that it is, as it were, crowded back upon the heart; this is the most satisfactory explanation of the cardiac hypertrophy. Compensatory hypertrophy is necessitated and developed to overcome the increased obstruction, independent of any change in the renal circulation. Its frequency in the sclerotic variety is unquestionably due to the longer existence of the renal blood and vascular changes.

In the parenchymatous group and those of short duration, hypertrophy is not the rule. It has also been claimed that the changes in the heart wall are due to the urea, which is more abundant in the blood, and that it acts as a direct stimulus to the cardiac muscle, and in this way the hypertrophy can be explained. Unfortunately for this theory, it is pretty generally admitted that, in the condition known as uræmia, the cause is not the retained, but the deficient production of urea. What actually produces the uræmic symptoms has not been clearly demonstrated; but it is some intermediate and incompletely formed product of proteid metabolism. Until we can ascertain to a certainty what the irritating substance is, it will be impossible to determine its influence upon the heart.

(*b*) Organic valvular lesions may have existed prior to any renal lesion, and in some cases produced a chronic congestion which ultimately resulted in a fully established and chronic kidney disease. This condition has been termed a cyanotic kidney. In such a case as this, the renal lesion is the complication to the cardiac disease.

(*c*) On the other hand, the deteriorated condition of the blood, with its contained irritants, may excite an endocarditis which in turn is followed by organic valvular changes. Now the cardiac lesion complicates the renal disease, and in all these instances the prognosis is more serious than with either alone.

(*d*) In many instances, the necropsy will reveal a soft, small, and atrophied heart. This is true of the third form of chronic diffuse

nephritis and the parenchymatous group, and this is due to the progressive and general mal-nutrition.

The cardiac lesions are to be treated on the general principles which govern those diseases, independent of the renal lesion. Anything which improves the condition of the heart will relieve the kidneys and cause the general condition of the patient to improve. One of the best cardiac tonics to stimulate the heart's action and increase its nutrition is the following:

R Tincturæ Opii Deodorati............. .... ℥ iij.
  Tincturæ Nucis Vomicæ...................... .... ℥ ss.
  Tincturæ Belladonnæ .... ℥ iij.
  Tincturæ Gentianæ ....q. s. ad ℥ iij.
M. Sig. ℥ i. *ter in die.*

(*i.*) *Cirrhosis of the Liver.*—This condition may be present at the same time as the renal lesion, but usually precedes the kidney trouble. Interstitial hepatitis is more likely to occur with, or act as, the cause which produces the chronic parenchymatous metamorphosis of the kidneys. When it occurs with the diffuse or sclerotic form, it is a coincident lesion. When the two coexist, the interstitial hepatitis greatly impairs the digestive function of the liver, and increases the amount of work to be performed by the excretory structures of the kidneys, and in this way it renders the prognosis more unfavorable.

For this condition of the liver little can be done in the line of therapeutics. The food should be plain and nutritious, and all hepatic irritants should be avoided.

(*j.*) *Constipation and Diarrhœa.*—A form of obstinate and chronic constipation and a kidney lesion often coexist. This condition may be regarded as a uræmic constipation, which is produced by the renal disease. It is often very persistent, and refuses to yield to any form of cathartic, elaterium and croton oil not excepted. It is believed to be due to a paralysis of the muscular tunic of the intestine, which is brought about by the depressing effects of the so-called uræmic poison, whatever this may be. In this way a persistent paralysis of the intestinal muscular fibres is produced. In other cases, there is an equally persistent diarrhœa, or the two may alternate. The constipation, however, is the more serious, and carries with it greater danger to the patient.

This complication is very intractable, and by preventing free elimination from the alimentary tract, naturally endangers life. Large and repeated doses of nux vomica, alone or in combination with belladonna, are very serviceable, especially in the chronic forms.

This condition often becomes very troublesome for a few days or even weeks just prior to death, and causes general distress from the accumulation of a large amount of gas within the intestine. An obstinate constipation, with suppression of urine, frequently occurs, and if not relieved, must produce a fatal issue.

A certain method for relieving these severe symptoms is by the hypodermatic administration of the muriate of pilocarpine, three-fourths of a grain being given at once. It is also well at the same time to administer cardiac stimulants. This plan of treatment will set all the excretory organs in motion and often prolong life. If full doses of elaterium or other cathartics have preceded the pilocarpine, the symptoms may become alarming, but the patient will ultimately be relieved, a mishap having never been witnessed.

If the intestinal distention becomes very great, puncture with an aspirating needle or trocar and cannula may be practised, or a rectal tube may be inserted and the gas allowed to escape.

(*k.*) *Eczema.*—This variety of skin lesion is occasionally associated with a kidney lesion. It is exceedingly annoying to the patient, and does not readily yield to treatment. The incessant irritation renders it a serious complication. It may be recovered from, but more frequently terminates in an erysipelatous inflammation or gangrene, and in this way acts as one cause of death.

It must be treated upon the principles which govern the management of all forms of eczema, but an improvement of the renal disease is the chief thing.

(*l.*) *Emphysema.*—This lesion of the pulmonary tissue is by some observers regarded as a frequent complication. It, however, does not appear to be traceable in any direct manner to the renal affection, but is another coincident lesion.

Little can be done for it in the way of treatment, except to keep the respiratory tract moist and free from mucus.

(*m.*) *Endocarditis.*—This, with the lesions of the valves produced by it, is a decided and one of the most serious complications produced by renal disease. This inflammatory condition of the endocardium is believed to be caused by the irritating condition of the blood.

Its treatment is that of the kidney disease. If the renal lesion can be improved, the quality of the blood will also improve, and the endocardial lesion will subside or disappear.

(*n.*) *Erysipelas.*—This is a rare complication. It may develop spontaneously, or be secondary to an erythematous or eczematous inflammation of the skin; and in some instances it follows directly upon the puncturing of the integument for the relief of the excessive œdema.

It is said to be a frequent result of these incisions, while others consider it an infrequent occurrence. It, however, does occur in some cases, and is always to be considered before resorting to the operative method for the relief of the excessive œdema. When developed, it almost always hastens the fatal issue, and little can be accomplished in the way of treatment.

(*o.*) *Gangrene.*—This may follow the eczema or erysipelas, or be developed independently and of itself prove a rapidly fatal complication.

Treatment is of little avail. Such cases usually terminate in a few hours, or days at the outside. To overcome the unpleasant odor, the affected part should be packed in Fuller's earth.

(*p.*) *Gastric Affections.*—There may be only an irritability of the stomach, functional dyspepsia, or there may be a more pronounced catarrhal condition with marked anatomical changes. The disease may be acute, subacute, or chronic.

The muscular tunic of the stomach may be hypertrophied or atrophied. But the morbid changes are more frequently located in the mucous membrane. The interstitial tissue surrounding the gastric follicles is infiltrated and thickened, and with this there may be either an hypertrophy or atrophy of the glands; in the majority of the cases, it is the latter, which is associated with a parenchymatous transformation of the protoplasm of the epithelial cells lining the tubules. The smaller vessels of the stomach may be the seat of miliary aneurisms or of a hyaline infiltration. The latter, however, is rare, unless the renal lesion be associated with prolonged suppuration and continued syphilitic manifestations, probably the latter.

In all forms of kidney disease, gastric irritability is liable to be developed.

Symptoms referable to the stomach are quite common in all the acute forms, and with each exacerbation in the chronic forms. When the gastric symptoms continue for a long time and do not yield to treatment, even in the absence of other renal symptoms, they are strongly indicative of the existence of a sclerotic kidney.

This is doubly true if the patient passes an abnormally large quantity of urine with a low specific gravity.

These manifestations are, strictly speaking, a part of the original disease, and the lesion of the stomach only acts as a complication when it decidedly interferes with digestion and assimilation.

The symptoms are produced in one of three ways, or by their combined action, viz., by an attempt on the part of the gastric epithelial cells to eliminate the effete material which should be removed by the

renal organ. In this way the peripheral ends of the nerves are constantly irritated and cause the symptoms; or the hyaline infiltration of the vessels may impair the nutrition of the membrane and the peripheral nerves. But in the larger number of instances, it is best explained and accounted for by the central irritation of the nervous system, which is constantly being irritated by the incompletely formed products of tissue metamorphosis circulating in the blood. The severity and persistence of the nervous manifestations will depend upon the duration of the disease and the amount of damage done to the renal excretory apparatus. If the renal cells can be made to regain their power of elimination, the nervous symptoms, by the aid of nerve tonics, will diminish in severity or disappear.

The gastric symptoms can be treated by all the stomach and dyspeptic remedies, but as long as the effete material circulating in the blood is allowed to remain, their efficacy will at best be slight.

The only hope for relief is in removing the cause. This set of symptoms is most easily and speedily relieved by the eliminative treatment with elaterium.

The result of this is to carry out of the system a large amount of the poisonous products of tissue waste, and at the same time diminish the amount of work required of the kidneys. The nutrition is improved and the renal glands are given a chance to repair the damage already sustained. By following this plan, with a judicious use of diuretics and diaphoretics, the renal lesion in many instances can be materially improved, and the unpleasant symptoms held in check for months, and in some instances for years.

Pilocarpine and diuretics are of service in severe and acute attacks. Counter-irritation at the scorbiculis cordis always gives some relief.

(q.) *Hemorrhage.*—The rupture of the miliary aneurisms already described, or of a large aneurism, may cause a fatal hemorrhage.

(r.) *Hepatic Disease.*—Functional hepatitis. This condition has been classed as a complication, but more accurately speaking it is primary, and one of, if not the most frequent, causes for all forms of renal lesions. Preventing as it does the complete transformation of the nutritive and excretory substances, it causes an incomplete nutrition throughout the body, and increases the quantity of effete and irritating materials in the blood, thus increasing the amount of work to be performed by the kidneys. When of short duration, as occurs in connection with the acute infectious diseases, an acute parenchymatous lesion will be established; but when of longer duration, a chronic metamorphosis will result, and continue as such until death, or a chronic diffuse nephritis may be established.

The advanced renal metamorphosis, in connection with diabetes, is a typical illustration of a kidney lesion secondary to a disturbed and incomplete hepatic metabolism.

The *treatment* of the functional hepatitis, occurring either primarily or secondarily, requires the closest attention.

In this form of hepatic disturbance, the bile pill mentioned on p. 26 will be found of special service; also the general nerve tonic, p. 89.

(*s.*) *Hydropericardium.*—Cardiac dropsy occurs as a part of the general anasarca, or it may be developed in cases where there has been no previous general œdema. It is always a serious and often a fatal complication, compressing as it does an already weakened heart. The spontaneous variety without previous dropsy is the more dangerous.

The *treatment* for this condition is to produce a rapid elimination by the skin, bowels, and kidneys, and corresponds closely with that for general anasarca. Brisk cathartics, with the administration of cardiac stimulants, such as ammonia, Hoffmann's anodyne, and alcohol, will be found the safest and most effectual treatment.

(*t.*) *Headache.*—This is sometimes classed as a complication, but it is not so, strictly speaking, but simply an aggravated symptom.

It is produced by the irritating influences of the retained effete material in the blood upon the nerve centres.

This will sometimes yield to iron preparations, to quinine, to the application of hot or cold water, or the two alternately. The breaking of a pearl of amyl nitrite in the mouth will, in many instances, give temporary relief. Many drugs will dispel the pain for a time, but they all fall short of permanent cure. In some of the severer types, morphine may be called for, and its use justified, but great caution should be exercised in using it, for it is not as safe as some have advocated, and occasionally may be the cause of a fatal coma.

The following will often give relief and prevent the necessity for using morphine:

 ℞ Chloroformi et
  Tincturæ Aconiti............................āā ℥ i.
  Chloralis Hydratis et
  Pulveris Camphoræ ....āā ℥ i.
 M. Sig. External use.

This solution applied locally will often give relief and prevent the necessity for using morphine; it is best applied by saturating a cloth with the fluid and binding it on the part where the pain is most intense, and this can be repeated a few times if at first it does not produce the desired effect.

Eliminating the original poisons which produce the cerebral irrita-

tion is the only sure method by which a permanent relief can be expected. The prognosis in regard to the headache depends wholly upon our success in increasing the excretory powers of the system.

(*u.*) *Hydrothorax.*—This, like the pericardial effusion, may be a part of the general anasarca, or an independent affection. If there be much fluid effused into the pleural cavity, it will compress the lung and cause serious dyspnœa, and in some cases materially interfere with the movements of the heart. When developed independently of any general dropsy, it may excite an œdema of the lungs, and in this way, cause a sudden and fatal result.

Occasionally the pleuritic effusion may necessitate a paracentesis, but, as a general rule, it can be modified or caused to disappear by the use of cathartics, diuretics, and diaphoretics, aided by a fly-blister, all being used at once.

(*v.*) *Intestinal Catarrh.*—The same causes which disturb the stomach act in a similar manner upon the intestinal tract, and induce a catarrhal condition which produces a diarrhœa alone, or with an alternating constipation.

This condition must be treated upon general principles, remembering always the eliminating part.

(*w.*) *Jaundice.*—Functional derangement of the liver may be developed at any time during the course of a renal disease, and give rise to varying degrees of jaundice and constipation with clay-colored stools which, by throwing more work upon the kidneys, materially complicate the case, and should be relieved as speedily as possible, by using cholagogue cathartics, such as calomel, podophyllum, phosphate of sodium, etc., or by tonic cholagogues, such as small doses of mercury, ipecacuanha, etc.

By a tonic cholagogue is meant such drugs or mineral spring waters as have a tendency to increase the quantity and quality of bile produced. The one which most closely imitates nature is the ordinary ox bile. By giving a few grains of the inspissated bile, great relief will often follow.

A cathartic cholagogue is a remedy which sweeps all excess of bile from the alimentary tract. In this form of hepatic derangement the following pill is especially applicable:

R Hydrargyri Chloridi Mitis ....gr. iij.
Fellis Bovis Inspissati.....................gr. xxiv.
Quininæ Sulphatis ....gr. xij.
Extracti Taraxaci........................ ℥ ss.

M. et fiat massa in capsulas no. quindecim dividenda. Sig. One *ter in die* before meals.

(x.) *Meningitis.*—A form of chronic thickening of the pia mater, or chronic meningitis, is frequently associated with all renal lesions which last for any length of time. From a pathological, if not from a clinical standpoint, it should be regarded as a complication, and probably is one factor in causing the continuous headache of kidney disease.

This lesion is not generally amenable to treatment.

(y.) *Neuro-retinitis.*—A chronic inflammation, involving both the optic nerve and retina, is met with in some cases of renal disease, especially in connection with the chronic diffuse nephritis and the sclerotic varieties. It may cause dimness of vision, and even blindness. It requires no special treatment, for when the nephritic disease improves, the same is true for the eye symptoms. A similar condition may be developed with other diseases, so that, taken alone, it cannot be considered as diagnostic of renal trouble.

(z.) *Œdema of the Lungs.*—This pathological change usually occurs at some time in the course of the disease. It may develop early in the acute stage; with an acute exacerbation, in connection with a chronic lesion, or it may not occur until late. It may be the determining cause of death, and usually occurs at the end of every case. It is caused by the general hydræmic condition of the blood, through the nervous system, and as the result of cardiac failure. The symptoms which it gives rise to are rapid and shallow breathing, dyspnœa, and cyanosis. Physical examination reveals sharp, crackling, subcrepitant râles over the dependent portions of both lungs, which are often more marked upon one side than the other. These attacks are frequently repeated during the course of some cases, and, unless promptly treated, may result in an untimely death.

Treatment.—At the time of the attack, a number of dry cups should be applied to the chest, with the internal administration of volatile cardiac stimulants. This should be followed by the more permanent stimulants, tonics, and eliminating agents, applicable to a general dropsy.

(aa.) *Œdema Glottidis.*—This affection occasionally occurs either as part of the general œdema or as a separate and distinct lesion. It gives rise to sudden and dangerous symptoms, characterized by an inability to inhale air and a rapidly developing cyanosis, the expiratory act remaining unaltered. When developed, unless immediately relieved, it will terminate the life of the patient.

The treatment consists in the scarification of the œdematous arytenoepiglottidean folds, or in the performance of tracheotomy. The former is to be preferred if it can be accomplished with safety. The

laryngeal intubation, as recommended by Dr. Joseph R. O'Dwyer,[1] might be applicable in some of these instances. Dr. Samuel Lloyd has noticed that the diminution in the œdema is often followed by a dislodgment of the tube, and if the physician is not on hand to reinsert it or introduce a larger tube, a recurrence of the œdema is the rule.

(*bb.*) *Œdema.*—General dropsy, or anasarca, when excessive, may be spoken of as a complication.

The treatment of the condition is by diuretics, diaphoretics, and cathartics, Esmarch's elastic bandage, and a free use of cathartic remedies, as before explained (page 37). In extreme cases, it may be found necessary to puncture the integument, and allow the serum to drain away through the openings, but this is only justifiable as a last resort. Rather than permit the extensive sloughing, which otherwise is likely to ensue, it would be much better to undertake this operative procedure even though the danger of the development of erysipelas and gangrene is great; the latter is almost certain to occur if the extensive œdema remains untreated.

(*cc.*) *Pericarditis.*—This, like endocarditis, is developed during the course of a renal disease.

It seems to be excited by the irritating excretory products contained in the blood, and may be the first indication of the existence of a renal complication. When it cannot be traced to rheumatism or some other acute disease, the urine should always be carefully examined, and in a large proportion of cases albumin and casts will be found.

The treatment consists first in removing the exciting cause, to be followed by the principles applicable to pericarditis in general.

(*dd.*) *Peritonitis.*—Inflammation of the peritoneum also suggests a urinary analysis, for it is excited in the same way as the pericarditis.

Opium, preventing free elimination by the alimentary tract, naturally throws more work upon the kidneys, and while it may decidedly improve the peritonitis, it increases the strain upon the renal organs, and materially interferes with their treatment. The question naturally suggested is, " Will the kidneys' epithelium stand this extra strain ?" In very many instances, it will not, but a uræmic toxæmia is developed, which terminates the case. During such a course of treatment, free diaphoresis and diuresis must be maintained, and the kidneys given every possible chance of accomplishing this extra work.

The above remarks are especially applicable in connection with

[1] New York Medical Record, Aug. 25th, 1885.

abdominal surgery.   It has been found at several necropsies in
which death followed an abdominal section, that the incision in the
abdominal wall and the intraperitoneal wound was in a state indi-
cating a rapid reparative process and not one of a septic nature.   At
the same time, the patients had died with symptoms which are com-
monly classed as septicæmic.   Close investigation, however, revealed
the fact that these toxæmic symptoms were due to a rapidly develop-
ing acute parenchymatous metamorphosis of the kidneys.   In every
instance, the bladder contained urine in which albumin and casts
were abundant and characteristic of this acute parenchymatous lesion.
The microscopic sections made from the kidneys revealed the finely
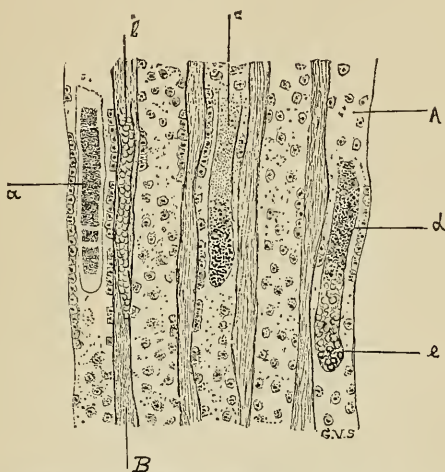
FIG. 19.—ACUTE PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEY FOLLOWING A PRO-
LONGED SURGICAL OPERATION.   × 350.

A, Collecting uriniferous tubule showing degenerating and desquamating epithelium and a
cast in the lumen; a, hyaline cast in the lumen of a collecting tubule; B, intertubular tissue
thickened by an œdematous swelling; b, blood-vessels containing blood-corpuscles in the inter-
tubular tissue; c, granular cast in the lumen of collecting tubule; superior extremity finely
granular, inferior extremity, or that nearest the apex of the pyramid, coarsely granular; d, e,
cast in tubule; d, internal end, coarsely granular; e, external end in a state of fatty metamor-
phosis.

granular metamorphosis common to this form of lesion ; and in many
instances casts were found in the lumen of the collecting tubules.
    Clinical observation upon this particular point or lesion has shown
quite conclusively that in all major surgical operations, but especially
those in connection with abdominal surgery, there is a strong ten-
dency to the development of an acute parenchymatous metamorphosis
of the kidneys.   The evidence of this lesion usually appears on the
second or third day after the operation, when the quantity of water

decreases, the color deepens, the specific gravity increases, and albumin and casts become more or less abundant.

If at this point active treatment be instituted with copious draughts of simple or medicated water, the quantity of urine voided will be increased, the albumin and casts will be diminished or disappear, and at the same time the specific gravity will fall; if attention is not devoted to this condition, and if active treatment is not instituted, the septic symptoms will continue, and the cause of death will be a uræmic toxæmia.

Careful observations upon this point were made at the Presbyterian Hospital by the late House Surgeon, William W. Sherman, especially for this section, who found in several instances this peculiar train of symptoms in connection with severe surgical conditions.

The case in which Prof. William F. Fluhrer ligated the common iliac, and in which an active renal lesion was developed and confirmed by the necropsy, is another instance of the same kind.

The way in which this lesion is produced is as follows:

First. We have the irritating effects of the anæsthetic, together with the primary shock of the operation, both of which have a strong tendency to disturb the nervous mechanism, and in this way alter and render imperfect the metamorphotic processes of the body, and thus increase the amount and irritability of the effete products to be eliminated.

The damage to the system which results from the administration of ether is induced as follows:

The anæsthetic action is principally, if not exclusively, brought about by shutting off from the system the normal quantity of oxygen, which causes the blood to become surcharged with carbon dioxide (CO_2). In fact, all the anæsthetics appear to have their chief action in their property to deprive the system of oxygen, for it is well known to all that anæsthesia cannot be produced so long as the system receives its requisite quantity.

This diminution of oxygen of necessity interferes with the chemico-physiological metamorphosis of the body, decreases or arrests nutrition, poisons the system, and increases the amount of work to be accomplished by the liver and renal glands.

Experiments further go to show that ether has the property of destroying the red blood-corpuscles, which is also a damage to the blood, and causes the body oxidation to be less complete, so that the products of tissue metamorphosis to be eliminated are very irritating to the renal epithelium.

The nutrition of the kidneys at the same time is very much diminished or totally arrested. The nervous system is in a state of partial shock attendant upon the operation.

In the majority of surgical cases, the duration of the etherization is short, and the operation a slight one. In these the system easily sustains the damage and completely recovers.

But in the minority, the etherization is prolonged, and the operation severe, or a vital part of the body is implicated. Now the prolonged decrease of oxygen and great increase in carbon dioxide (CO_2) in the blood, together with the destruction of the red blood-corpuscles, so impairs the nutrition and elimination of the liver and renal glands that a uræmic toxæmia is developed, the symptoms of which have erroneously been called septicæmic.

These important facts, substantiated by a large number of necropsy examinations, tend to prove that ether is not a perfectly harmless agent. They also teach that the period of etherization should always be as short as possible, if the greatest success is to be attained.

The above is not an argument in favor of chloroform, for it has all the dangerous effects of ether, as well as an unavoidably depressing effect upon the heart, while ether appears to stimulate this organ, thus enabling the system to withstand its ill effects, except when it is unduly prolonged.

Second. There is also an increase in the amount of effete material to be eliminated, as a natural sequence to the increased nutritive activity necessary for the reparative process.

Third. The often unavoidable use of opium for the relief of pain interferes with the hepatic functions, and in part closes the excretory apparatus of the respiratory and alimentary tract, especially the latter, and thus forces more work upon the skin and kidneys. For these reasons, the metabolism becomes excessive and incomplete, its products imperfect and very irritating to the excretory organs, and especially so to the renal epithelium. As a result, this acute parenchymatous metamorphosis is established, followed by the so-called septic symptoms which, in the strict sense of the word, are uræmic, or the result of defective elimination.

The development of this lesion easily explains many of the " septic symptoms" which are developed within a few hours or days after an operation, and which quickly, and almost without warning, terminate life. It often happens in these cases that the original wound is apparently progressing favorably, there being no suppuration nor anything about it to account for the septic condition. Not infrequently, the urine examined prior to the operation is found to be normal,

while that taken from the bladder forty-eight hours after the operation is found to contain albumin and casts in abundance, and sections made from the kidneys always reveal the changes characteristic of an acute parenchymatous metamorphosis of the renal glands.

These pathological, together with the clinical facts, carefully noted by Dr. Sherman, prove quite conclusively that the above method of development is the true explanation for these cases.

The urinary changes have been ascribed to the disturbed renal circulation, but it seems more reasonable to attribute them to the disturbance of the system at large; and if to any vascular area alone, to that of the liver. For the septic symptoms do not occur immediately after the operation, but after some hours, or one or two days have elapsed. With acute congestion of the kidneys and total suppression, albumin and casts do not always appear in the urine.

Having observed and studied a large number of these instances, the theory has been developed that, in all surgical cases having any gravity, the renal organs *demand* especial attention, and should always be prepared ahead for this severe and extra strain.

Having established the fact that renal lesions are quite frequently excited by severe surgical conditions, it suggests, not only the importance of examining the urine prior to every operation, but shows the great necessity for carefully analyzing the urine daily during the height of every surgical case, and also during the period of convalescence, if the early development of this class of renal lesions is to be recognized.

Treatment.—For a few days prior to all severe operations, fluids and non-irritating diuretics should be freely administered, for the purpose of washing out the uriniferous tubules, of improving the nutrition of the epithelial cells, and of placing them in the best possible condition to accomplish this extra work without becoming seriously impaired. During the height of every surgical condition, the renal organs should receive particular attention, and especially when the ether has to be given for a long time, and still more so if opium has to be freely administered; for it is much easier to prevent than to combat the lesion when fully established.

In treating the peritoneal complication of chronic renal lesions, the above facts must always be remembered, otherwise, by the use of opium, we may add an acute to a chronic renal affection, and render death inevitable.

(*ee.*) *Phthisis.*—Pulmonary tuberculosis may occasionally be associated with kidney disease. By some, it is thought that it is induced by

renal lesion. This may be true, but it is probably quite rare. Its treatment is the same as under ordinary circumstances, and the termination is always fatal.

(*ff.*) *Pleurisy.*—An inflammation of the pleura may be induced by the uræmic condition of the blood, in the same way that the other serous membranes are attacked. The inflammatory process may be acute or chronic; it, however, is more likely to be of the subacute variety, producing a serous exudation. If the effusion be considerable, it compresses the lungs, and often produces a very marked dyspnœa, and then acts as a serious complication.

It may be *treated* by the various eliminating agents. A large fly blister over the affected side, with free catharsis and diuresis, will usually cause the fluid to be absorbed, but all three must be used at the same time to secure the desired result.

(*gg.*) *Pneumonia.*—All forms of chronic pneumonia are met with in connection with chronic kidney lesions, but they frequently precede the renal disease, and are not induced by it. Nevertheless, they act as complications when present.

The acute or lobar pneumonia unquestionably acts as a direct cause in producing an acute parenchymatous metamorphosis of the kidneys, and may be one of the remote causes in producing chronic renal lesions. This form of pneumonia often occurs in connection with chronic kidney disease, but it is impossible to say that it is directly excited by the renal affection, or that these patients are specially predisposed to lobar pneumonia. One thing, however, is quite certain, that, whenever it does occur in this connection, the prognosis is always bad. The only method of *treatment* is free and early cardiac stimulation by the ammonia salts and alcohol, which should be administered at short intervals, and often in very large doses. No specific dose can be given, but the pulse or heart's action must be the guide. Stimulants should be pushed until the pulse falls in frequency and increases in force. Ergot will also be found of service in that it steadies the contraction of the arterioles, and renders the general tension more even. Opium would be more effectual for this purpose if it did not prevent elimination.

By the above method of medication, and the frequent use of dry cups to the chest and loins, many cases will recover which otherwise would terminate fatally. Warm poultices applied to the loins often aid in keeping the kidneys active.

Digitalis should be avoided in these cases, as it is apt to cause heart failure.

(*hh.*) *Retinal Lesions.*—There may be a simple retinitis without
6

involvement of the optic nerve; this, however, is rare. A more fre-
quent condition is a retardation of the capillary circulation with a
tortuosity of the retinal veins; and a dropsical effusion into the disc
tissue ("choked disc"): with this there may be a secondary inflamma-
tory effusion and cellular proliferation, or fatty degeneration with the
formation of white elevated spots. There may also be found apoplec-
tic extravasations, emboli or thrombi of the retinal veins. These
lesions may be followed by atrophic changes in the substance of the
retina. All these changes may occur without impairment of vision,
but, whenever they are located within the field of vision, there will
be some impairment of sight. At one time certain lesions of the
retina were thought to be almost pathognomonic of renal disease, and
were described as albuminuric or nephritic lesions of the eye.

(ii.) *Uræmia.*—A peculiar train of nervous manifestations is de-
scribed under this name. It may be considered as a separate disease,
as a set of aggravated symptoms, or as a complication of the kidney
lesions. The latter is the one preferred, as uræmia is always second-
ary to some renal change, and a new factor invariably comes in
between the organic lesion and the uræmic symptoms.

It is this intermediate factor which has given rise to an endless
amount of discussion *pro et con*.

The diseased conditions in which uræmic symptoms are developed
are now pretty thoroughly understood; but the exact nature of the
uræmic poison, and the *modus operandi* between its development and
effect, is as complete a mystery as ever.

Many theories have been advanced and as frequently refuted. One
fact, however, has been quite thoroughly established, which is, that
in every instance there is a diminished quantity of urea in the
urine, and at the same time there is not a proportionate increase of
the urea in the blood. Neither does the injection of urea into the
blood produce uræmia. The toxic consequences, therefore, do not
appear to be dependent upon the presence of urea in the blood, but
to some other and as yet incompletely defined product of tissue
metamorphosis, which the kidneys are not calculated to eliminate
from the system as speedily as is required.

Numerous experimental researches have been instituted, but very
little exact information has resulted.

One condition is pretty generally accepted, however, which is, that
urea alone is not the cause of the symptoms.

Frerichs believed that the decomposition of urea in the blood into
carbon dioxide (CO_2) and ammonium carbonate accounted for the
trouble. This idea has been disproved by repeated injections of

carbonate of ammonium into the blood without producing any uræmic symptoms.

The ammonia theory is also disproved by experiments which go to show that no urea was present in the blood from which the carbon dioxide and carbonate of ammonium could have been developed.

Some experimenters believe that kreatin, either alone or in combination with some undiscovered and incomplete product of tissue metamorphosis, is the true excitant.

Again, Traube advanced the theory that it was purely a mechanical process, due to an œdema of the brain brought about by a varying blood pressure.

This also has been proven to be erroneous, the œdema being a result and not a cause.

Much valuable time has been expended in experimental research, and in developing new and ingenious theories, but as yet the exact irritant has not been defined.

Until the physiologist or the pathologist, or both with their combined efforts, can more clearly elucidate the chemico-physiological changes going on in the body between the introduction of the nutritive elements, the tissue metamorphosis, the elimination of the resulting products, and their action upon the system in their incomplete and intermediate state, the subject must in a measure remain *in statu quo.*

From the varied manifestations which are attributable to this form of blood-poisoning, it would appear that they cannot be traced to any single element. But that there are a number of poisonous substances developed during the tissue metamorphosis and the complete formation and elimination of the urea is undoubtedly true. Depending upon the predominance of one or the other of these irritants, we can easily explain and appreciate the great variety of symptoms classed under this common term.

The uræmic symptoms are often very indefinite, and too numerous to mention in complete detail. Their onset is very uncertain. They may develop as an indefinite and chronic form, or they may be acute and decisive in their nature from the commencement. In the former case, the symptoms are often vague.

There may be general or localized muscular twitchings which, in either case, may be mild or severe from the first.

The voluntary movements are impaired, uncertain, and sluggish; this is also true in regard to some of the involuntary, especially noticeable in the alimentary tract; the heart is often enfeebled in its action; sight is often dim and in some cases approaches to blindness; tinnitus

aurium and severe headaches are quite frequent. Dyspnœa, nausea and vomiting, diarrhœa or relaxation of the bowels, alternating with persistent constipation, are not infrequent. Active delirium, convulsions and coma may close the scene. One or more of this list of symptoms may be the first to appear and persist alone for a long time: or it may be of short duration, and then disappear to recur or be replaced by another, or by a group of symptoms, all of which are produced by these indefinite blood poisons. In this way a very great variety of symptoms are developed in a single case, which often leads to an error in diagnosis.

These remissions and exacerbations are repeated many times, but as the organic lesion progresses, they become more and more pronounced, and terminate the case in an *acute exacerbation*, or *more gradually deepen into coma*, to which the patient finally succumbs.

On the other hand, they are acute and decisive from the very onset, and are divisible, from a clinical standpoint, into three sets of cases:

(*a*) Those that commence with severe convulsions, and terminate in them, or rapidly pass into coma, to be followed by death.

(*b*) Those in which the coma develops suddenly, and speedily terminates life.

(*c*) Those in which the comatose and convulsive stages are more or less intermixed, neither absolutely predominating.

(*a*) The convulsive variety is most frequently met with in connection with the sclerotic and gouty forms of renal disease, although it may occur with any variety. Such an attack may be only an exacerbation of the chronic state, or it may appear without any previous warning. If the case has been closely watched, a slight elevation of temperature will be found to precede the attack. In some instances, the convulsions are general, and in this respect closely resemble an epileptic seizure, so that during the attack it is occasionally difficult to differentiate between the two. A careful inquiry, however, into the previous history, and an examination of the urine will usually decide the question. In other cases, the convulsive symptoms will be limited to certain groups of muscles, and closely simulate tetanus.

The face in either case is usually blanched, but occasionally it may be flushed over the malar processes; the conjunctivæ may be injected, but more frequently they are pale and glassy; the pupils at first are contracted, but later in the attack, the larger proportion are dilated. The urine is often scanty, and occasionally suppressed. Frothy mucus, sometimes tinged with blood, collects in the mouth and around the lips. The integument is dry or moist, but, as a rule, a strong urinary odor emanates from the body. The expired air frequently has a pecu-

liar odor, which is known as the uræmic breath. Some cases lose consciousness completely, while others retain their senses to the last.

This train of symptoms may last for fifteen or twenty minutes only, or be prolonged for several hours, occasionally terminating in recovery with no subsequent repetition, but more frequently death occurs at the height of a convulsion, or a fatal coma is developed.

Uræmic convulsions have to be differentiated from epileptic and hysterical seizures and apoplexy. From epilepsy they are distinguished by the previous history. There is no initial cry. The pallor and convulsions are more marked. Uræmia passes into coma; epilepsy is followed by sleep. The urine in uræmia usually contains albumin; rarely in epilepsy. In uræmia, the convulsions are equal on both sides; in epilepsy, they are more marked on one side.

From apoplexy, by the hemiplegia which follows the unilateral convulsions. In hysteria, there is often a cry, followed by convulsions and a tetanic or cataleptic condition.

The pupils, face, and temperature remain normal in hysteria, and the patient is always conscious. The limbs are jerked irregularly, the respiratory movements are spasmodic, and a choking sensation is often noted in hysteria, all of which are absent in uræmia. After the hysterical attack, large quantities of pale urine are voided.

(b) In the second or comatose variety, the symptoms develop without warning, or are preceded by slight cerebral symptoms, such as headache, dizziness, etc., which finally culminate in coma and death.

This condition may occur at any time during the course of a chronic uræmia. Each variety may be recovered from, and no recurrence follow. But, as a rule, it is repeated, and death follows in coma. Here again a slight elevation of temperature may be detected prior to the outburst. In all forms of uræmia, the temperature may run high or be below normal. The face is usually blanched, the eyes pale and glassy, the pupils contracted or dilated—as a rule, the latter—responding slowly to light. Occasionally a flushed face, injected conjunctivæ, and contracted pupils are witnessed. The breathing is of a peculiar hissing character, produced by the air striking forcibly against the hard and soft palate; it is not of the deep sonorous character which occurs in connection with apoplectic and opium coma. At first, the respiratory movements are accelerated, but soon they become slow and labored. The pulse is increased in frequency, and weak. The coma at first is incomplete, but at the end of a few hours is absolute, and the temperature falls to or below normal.

This condition has to be separated from apoplectic, opium, epileptic, and alcoholic coma.

The unilateral paralysis of apoplexy is the strongest guide; the face is also flushed and the pulse full and strong. In opium coma, the temperature is not altered, the pulse is full and strong, the face flushed and the pupils contracted, the breathing slow and stertorous, the reverse being true in uræmia.

From epilepsy, by the previous history and a urinary analysis.

From alcoholic coma it is often exceedingly hard; for the two are frequently associated conditions. In uncomplicated cases, the history and the strong alcoholic breath in one, and uræmic in the other, would easily determine the difference. The skin is cold and clammy in alcoholic, warm and often dry in uræmic coma.

(c) In that variety to which the term mixed has been applied, the convulsions and coma are so intermixed that it is often impossible to tell which was primary and which the leading feature of the attack. Further than this, the symptoms which may occur have all been enumerated in describing the preceding varieties. The prognosis and treatment will, of course, be the same. In some instances, the first and only symptom of the uræmic toxæmia is a paralysis of the heart's action.

The *treatment* of uræmia must be prompt and energetic. Free and repeated use of pilocarpine, elaterium, and hot-air baths, either dry or moist, are in order. The loins should be quickly cupped and followed by a poultice. Diuretics should be freely administered in the form of digitalis, caffeine, tincture of the chloride of iron, Hoffmann's anodyne, or the spirits of Mindererus.

A very good diuretic pill is the following:

   ℞ Caffeini..... .... ʒ i.
      Pulveris Digitalis................... ....gr. xl.
      Strychninæ Sulphatis ....gr. i.

M. et fiat massa in pilulas no. xx. dividenda.   Sig. One every three hours.

But for a quick action the following solution will be found very prompt and certain:

   ℞ Tincturæ Ferri Chloridi........................ ℥ ss.
      Spiritus Etheris Nitrosi et
      Liquoris Ammoniæ Acetatis. ....āā ℥ i.
      Aquæ ....q. s. ad ℥ iv.

  M.   Sig. ℥ ss. in a wineglass of water.

The bromides and chloral hydrate may be given with advantage in some cases; this is especially true in puerperal uræmia.

In this form, where the spinal centres are known to be more or less exhausted, large doses of morphine may be administered with advantage, but in most of the other forms of uræmia it will be followed by unfavorable results.

The puerperal cases, however, are best treated by general blood-letting, and inhalations of ether and chloroform are occasionally of service. In the more gradual or chronic forms, counter-irritation of the scalp or the nape of the neck is often followed by satisfactory results.

The use of morphine in the treatment of uræmia does not always seem to be safe, although this method has some strong advocates; while others tell us that it is demanded if there is reason to believe that the spinal centres are depressed, otherwise it is strongly contra-indicated; unfortunately they fail to inform us how we are to differentiate, in uræmic attacks, between the two conditions. The use of morphine, or any of the opiates, would seem, however, to be contra-indicated. The heart should be well stimulated, and œdema of the lungs carefully guarded against by dry cups over the chest. A further discussion of the treatment would be to repeat what has already been said in treating acute and chronic parenchymatous metamorphosis and other lesions of the kidneys.

(*jj.*) *Uræmic Blindness.*—This is a complication developed during the course of a renal lesion, in which there is no organic change visible, upon ophthalmoscopic examination, in the optic nerves or retinæ. The dimness of vision, amounting in some cases to total blindness, is due to the poisonous influence of the uræmic poison upon the cerebral optical centre. Permanent blindness may also result from a recognizable lesion of the ocular tunics or nerve.

In either case, little good results from any form of ophthalmic treatment, unless the original cause can be removed. Iodide of potassium has been highly extolled in these optic diseases; but its efficacy is probably due to the great frequency of latent syphilis in the human race, which is favorably influenced by this salt. The satisfactory results so often obtained from the use of iodide of potassium and small doses of mercury in the various forms of renal disease are unquestionably due to their influence upon this often undetected specific taint.

Treatment.—As the etiology of the group known as chronic diffuse nephritis is somewhat uncertain, little can be done in a direct line of prevention. This much, however, is known, that all excesses tend

to materially damage, not alone the renal organs, but every portion of the body. This fact is especially true during the period of life between the years of twenty and thirty. Having passed this period free from dissipation, and without any severe form of the acute diseases, the prospect for attaining a very old age without a renal disease is at its maximum. It seems reasonable, therefore, to suppose that repeated attacks of the acute diseases, which perhaps in themselves produce only a moderate amount of parenchymatous metamorphosis, nevertheless often pave the way for a chronic diffuse nephritis later in life. Consequently, it is the duty of every physician to prevent, so far as possible, the development of all acute diseases, and if they do become established, to guard the kidneys against the extra strain during such attacks. By so doing, the parenchyma of the kidneys may maintain its integrity, and the patient be protected from the development of a diffuse renal lesion later in life. This in itself will be a great gain in prevention. The chronic form frequently follows the acute, and here much can be done in the line of prevention, by simply avoiding the use of all irritant diuretics, many of which now stand first on our lists and are in daily use.

As climate is among the ascribed causes, the body should be well protected by woollen garments worn next to the skin; for in this way the sudden atmospheric changes have the least deleterious influence upon the system.

Cold often interrupts the normal metamorphotic processes of the body, and at the same time produces visceral congestion; in this way it greatly interferes with a complete proteid metabolism, and throws increased work upon the renal organs, producing a parenchymatous transformation of the renal cells, or a true inflammation of the whole organ. Bearing in mind this chain of events and guarding against them, the development or progress of this lesion may be prevented. In the chronic diffuse variety, although the method of production is not so clearly defined as in the parenchymatous group, the epithelial cells are involved and undergo a similar change; but in this lesion the nutrition of the cells appears to be primarily impaired, and the metamorphotic process is secondary. Even here the primary source of the trouble appears to originate in part in an incomplete action of the liver. It may be only a difference in the degree of the irritant, or it may be a difference in quality which determines the variety.

In all forms of kidney disease, there is a nervous element to be considered as well as the simple metamorphotic changes resulting from the increased eliminative action. The following mixture is

found to meet this indication both in relation to the liver and renal glands.

℞ Tincturæ Nucis Vomicæ.................... ... ℥ ss.
  Extracti Damianæ Fluidi .... ℨ vi.
  Tincturæ Gentianæ..................... q. s. ad ℥ iij.

M. Sig. ℨ i. *ter in die* after meals.

Or the same ingredients may be given in pill form.

℞ Extracti Nucis Vomicæ.....................gr. iv.
  Extracti Damianæ ....gr. xxxij.
  Extracti Gentianæ .... ℨ ss.

M. et fiat massa in capsulas no. xvi. dividenda. Sig. One *ter in die* after meals.

This form of nerve tonic stimulates both the motor and sympathetic nerves distributed to the liver and renal glands, which, together with the bile pills (page 26) and some form of iron, will, in many instances, cause a rapid and total disappearance of all the rational and urinary signs indicative of a renal lesion.

The two forms of iron which have been found most efficacious are the tincture of the chloride and the albuminate of iron lozenges, manufactured by Mr. Theodore Angelo, of this city. The latter are especially applicable, furnishing a certain amount of albumin with the iron.

In every case, severe mental or physical strains should be avoided, as they always render a renal lesion worse.

By carefully observing these laws, there will be the least interference with the physiological processes, the products to be eliminated will be more nearly perfect, and the kidneys will be the more likely to remain normal.

When the lesion has become fully established, the above rules apply with increased force in each and every particular. To prevent the dangers from the sudden changes in temperature, it is well for the patient to winter in a tropical climate. The fact that patients do better in warm climates, and the rarity of renal lesions both in the tropical and arctic zones, is strong proof that sudden change in temperature has a decided influence in damaging the renal organs.

The diet of patients suffering from a chronic diffuse nephritis should be composed of the most nutritious materials, and of those substances which are the most easily digested, absorbed, and assimilated; so that the products of tissue waste shall be as completely

formed and as little irritating as possible to the renal tissues in their passage from the blood to the urine. By these means the nutrition of the kidneys can be increased, and the destructive processes retarded, if not absolutely arrested. In this way life will be prolonged, and in some instances a cure be effected.

All stimulating condiments, excesses in alcohol, or in fact any kind of food or drink which is any way irritating or indigestible should be scrupulously avoided, as they all tend in the one direction—to retard nutrition and irritate the kidneys.

An exclusive milk, buttermilk, or skim milk diet is found to yield the best results in a majority of cases. Of the latter it is especially true. For the starches, sugars, and fats seem to be the principal factors in preventing a perfect proteid metabolism. It would be natural to suppose that a starch and fat diet, with a limited amount of the nitrogenous elements, would most completely overcome the difficulty, but experience teaches the contrary.

The hepatic cells in their weakened condition may be capable of transforming a sufficient amount of the albuminoids for nutrition and repair, but when the non-nitrogenous are added, they seem to be the first transformed, the hepatic cells become exhausted, and then the albuminoids are incompletely acted upon, and the renal lesion rapidly grows worse; in this way the action of the two is explained.

The medicinal remedies which have from time to time been extolled for their curative powers upon these lesions are not easy to enumerate. They have all proved about equally useless, and have little or no effect in directly bringing about a cure, except in so far as they aid in improving the general condition, and thus secondarily producing a reparative action upon the damaged renal elements.

The treatment of renal lesions, therefore, resolves itself into three general principles or divisions.

First, the prevention of all extra strains upon the system.

This part has been dealt with at length under the heading of prevention, and consists in aiding the system to perform the physiological metamorphotic changes with the least expenditure of force. When this is accomplished, nutrition is raised to its highest standard and the system enabled to produce considerable reparative material.

In addition to what has already been said, the use of tonics must not be forgotten. The best is the tincture of the chloride of iron, which assists in this result by increasing oxidation, and is also a good non-irritating diuretic.

Second, The accumulation of the effete and irritating substances in the system. These abnormal products interfere with nutrition

and the reparative, even if they do not hasten the destructive processes. Nature, therefore, must be assisted in every way possible to rid the system of these damaging products, which have to be eliminated largely by the kidneys.

This is best accomplished by a judicious use of diuretics, diaphoretics, and cathartics, as detailed on pages 35, 36, and 37.

Third. The treatment of the complications, as enumerated in the first part of this chapter. This often taxes the physician's therapeutic knowledge to the utmost, baffles every attempt, and quickly terminates the case by death. Some of the complications are fatal from their onset.

CHAPTER VI.

ACUTE AND CHRONIC SCLEROSIS OF THE KIDNEYS; GOUTY KIDNEYS; HYALINE, ALBUMINOID, OR WAXY KIDNEYS; SUMMARY.

SCLEROSIS OF THE KIDNEYS. CIRRHOSIS OR RED ATROPHY OF THE KIDNEYS.

FIRST FORM OF SMALL KIDNEY.

Definition.—A sclerotic kidney is one in which the primary lesion is almost exclusively confined to the intertubular tissue, which is very much increased in quantity and infiltrated with new cells. This newly formed tissue contracts and ultimately diminishes the size of the kidneys, · which are dark in color, their capsules thickened and adherent, and the underlying surface rough and granular. The afferent vessels have their walls thickened and the lumen expanded. There is no active lesion in the epithelial cells, but they are diminished by the pressure exerted upon them by the contraction of the new-formed connective tissue, which ultimately causes them to become atrophied.

An acute interstitial variety has been described by Professor Edward Delafield.[1]

" This is a rare form of nephritis of which the clinical history is still incomplete. One of its most noticeable features is that the patients may have marked dropsy and other renal symptoms without albumin in the urine.

" The kidneys are very large and succulent, the capsules are non-adherent, the surfaces are smooth, the cortex thick and whitish.

" The most marked change is the accumulation of white blood-cells in the capillary veins, and in the stroma between the tubules, while the epithelium of the tubes is but little altered."

Etiology.—The cause of this peculiar change, known as the chronic

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[1] " Handbook of Pathological Anatomy and Histology," Delafield and Prudden. William Wood & Co., 1885, p. 386.

form, has not been clearly elucidated. Some have given to it the same causes as for chronic diffuse nephritis, but these are unsatisfactory, because they do not explain the absence of the parenchymatous metamorphosis of the epithelial cells. It has been attributed to over-indulgence in alcohol, to rheumatism, cardiac hypertrophy, lead poisoning, etc. But there is no very clear connection in any of these instances, for it is quite as often developed in the absence of them all.

In many instances, the small forms of the diffuse group have

FIG. 20.—ACUTE INTERSTITIAL NEPHRITIS. × 850 and reduced. (Delafield and Prudden's "Handbook of Pathological Anatomy and Histology.")

undoubtedly been mistaken for sclerotic kidneys. This variety is only coincidently associated with the excessive use of liquor. There are comparatively few typical examples in which the clinical symptoms, the urinary manifestations, and the microscopic examination all coincide; but more frequently what is at first thought to be a cirrhotic kidney proves, clinically and microscopically, to be one of the atrophic forms of chronic diffuse nephritis. The results obtained from the study of a large number of necropsies have

demonstrated that it is the chronic parenchymatous lesion, if any, which can be directly traced to alcohol in excess.

The very common occurrence of tertiary syphilis, and its tendency to produce chronic thickening, may in a measure account for this lesion, if it is not the absolute cause.

It has been claimed that this variety is more frequent in females, but no special preference as to sex has been clearly demonstrated.

Macroscopic Anatomy.—The kidneys are very small, their capsules are thickened and closely adherent to the underlying renal surface, which, as a rule, is reddish in color, rough and often contains small cysts. The cut surfaces show the cortex to be thin and dark in color;
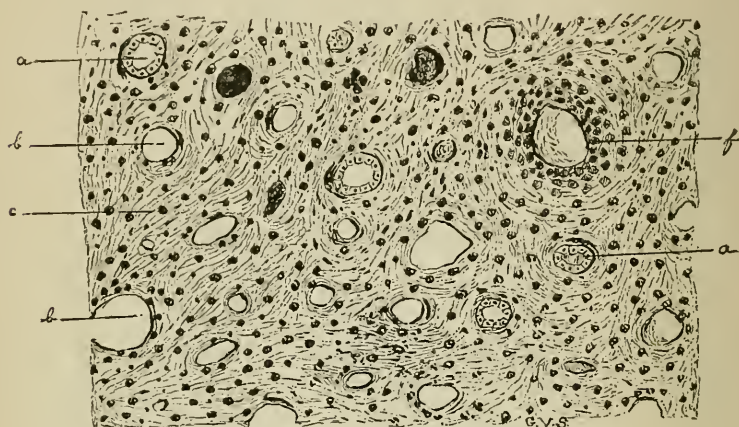

FIG. 21.—CHRONIC INTERSTITIAL NEPHRITIS. × 350.

a, Uriniferous tubules lined by normal epithelial cells; *b*, uriniferous tubules from which the epithelium has fallen out in mounting the section; *c*, dense fibrillated connective tissue studded with new cells; *f*, small arteriole thickened by a fibrous deposition known as the capillary fibrosis of Gull and Sutton. The large dark spots represent compressed and atrophied tubules.

the markings, if perceptible, are wavy, and the pyramids of Malpighi small and indistinct.

Microscopic Examination shows Bowman's capsule to be thickened, the Malpighian tuft often compressed and atrophied, the interstitial tissue between the tubes decidedly increased, and the walls of the vessels thickened and their lumen expanded. The epithelial cells are somewhat altered in character, but the change appears to be one of atrophy, due to the pressure exerted upon them by the contraction of the newly formed fibrillated connective tissue, and not to an irritation caused by the elimination of effete and irritating particles, or the effect of inflammatory exudation, as in the parenchymatous and dif-

fuse forms. In an advanced stage, the epithelial cells have undergone complete atrophy, the tubules have collapsed, and developed into connective-tissue bands, which appear under the microscope as fibrillated connective-tissue cords.

In the few typical examples of this variety of lesion, the atrophic changes were most marked near the apex of the Malpighian pyramids, and diminished from that point to the surface of the organ; but were more advanced at one end of the kidney than at the other. This observation suggested the idea that in this disease, for some unknown reason, the lesion began at one end and gradually swept around to the other, as pulmonary lesions extend from apex to base. If this be true, it would in a measure explain the indefiniteness of the symptoms and the sudden death.

FIG. 22.

Section showing thickened and expanded afferent vessel entering Malpighian tuft, the tuft being surrounded by a dense mass of fibrillated connective tissue. The open spaces represent transverse sections of the uriniferous tubules compressed by the new tissue, the epithelial lining having dropped out. × 350.

What epithelium there is left seems to be capable of accomplishing slowly and less perfectly the work which had been performed more rapidly by the normal kidneys. Some effete material is constantly retained in the blood, and naturally explains the vague nervous symptoms. A time comes, however, when so much of the epithelium has been destroyed that a sudden exposure or excess in diet causes an extra strain upon the already damaged organs, which is more than they are able to meet. They rapidly become overworked, paralyzed, as it were, and stop action; suppression of urine ensues, followed by convulsions, coma, and death, or the last may occur without total suppression.

Symptoms.—The systemic symptoms are very vague; in many in-

stances, when first seen, the patient is suffering from a uræmic con-
vulsion, or is in deep coma. Occasionally, he may come under obser-
vation as a dyspeptic, or suffering from dimness of vision, or with a
persistent and often intractable form of facial neuralgia, or an occipito-
frontal headache, or he may have a persistent dyspnœa without any
pulmonary lesions. In all cases presenting such symptoms, the urine
should be carefully and repeatedly examined. In this way an abso-
lute diagnosis can often be made, and the life of the patient prolonged.

The *urine* in this variety of renal lesion is always very much in-
creased in quantity, and the specific gravity is, as a rule, very low,
ranging from 1.010 to 1.005. The large quantity of urine is explained
by the hyaline or fibroid transformation of the smaller vessels. Al-
bumin is rarely found, but occasionally a trace may be detected; this,
however, is probably due to the slipping through of some of the
unassimalated peptones. Casts are not often seen, and are of no
marked significance, but occasionally a small hyaline cast may be dis-
covered.

The *diagnostic* points are the low specific gravity and the general
absence of albumin and casts, all of which persist for weeks, months,
or years.

Prognosis.—This is always a fatal lesion. By an early diagnosis
and the proper adherence to certain laws, life may be prolonged for
ten, fifteen, or twenty years—perhaps longer. In one case this lesion
was known to exist for fifteen years.

Treatment.—There is no medicinal remedy of any value, unless it
be the iodides and mercury. The patient should be made to thor-
oughly understand that the duration and usefulness of life depends
exclusively upon himself. His diet must be of the most nutritious
kind, and one easily assimilated.

All mental and physical excesses, as well as those of eating and
drinking, must be rigidly avoided.

Exposures of all kinds must be guarded against with an ever watch-
ful care.

This, however, will make life somewhat burdensome, but yields in
return a chance for many years of fairly good health, with sufficient
power for considerable work. But one thing must be remembered:
that a deviation from the above rules is likely to be followed at any
time, and almost without warning, by an attack of convulsions or
coma, from which they may be rallied, but which are equally liable to
terminate in death. This unpleasant issue may also ensue without
any apparent cause.

In some instances, a sudden paralysis of the heart is the cause of the

fatal issue, and such is the true explanation of the many recorded cases of death due to cardiac disease in which no apparent cardiac lesion is found at the necropsy.

Post-mortem observation in connection with the clinical history clearly demonstrates the fact that in some instances the uræmic toxæmia generates a poison which paralyzes at once, and without any premonitory symptoms, either the heart muscles or its nerve centre, and causes an instantaneous arrest of its function.

In other instances, a cerebral hemorrhage closes the scene.

The rupture of a miliary aneurism in the stomach or alimentary canal is occasionally the immediate cause of death.

GOUTY NEPHRITIS.

FOURTH FORM OF SMALL KIDNEY.

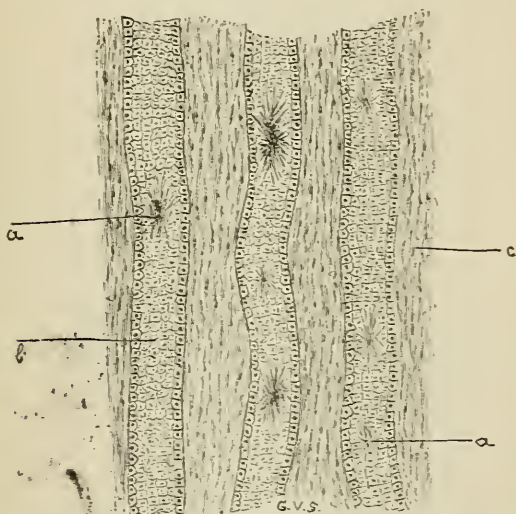*Definition.*—Kidneys in this condition do not differ in any re-

FIG. 23.—SECTION FROM A TYPICAL GOUTY KIDNEY. × 350.

a, Acicular crystals of sodium urate in the uriniferous tubules: *b*, uriniferous tubule, epithelium normal; *c*, fibrillated connective-tissue thickening between the tubules.

spect from those in the condition of sclerosis, except that masses of acicular crystals of sodium urate are seen in the uriniferous tubules. Similar crystals are also found in the urine. ·

Excepting that the disease occurs in connection with gout, it does not differ in its etiology, pathology, symptomatology, prognosis, and treatment from renal sclerosis.

In case the patient with gout should develop one of the forms of chronic diffuse nephritis, and have associated with it a similar deposition of acicular crystals in the renal substance, it might be classed as a gouty kidney.

This classification of gouty kidney is not a distinct and separate form, but is described in this way that the reader may more clearly appreciate its exact position.

The deposition of the sodium urate crystals is a secondary condition and indicates a gouty habit.

HYALINE, AMYLOID, WAXY, LARDACEOUS, OR ALBUMINOID KIDNEYS.

A FORM OF LARGE RED KIDNEY.

Definition.—The hyaline, amyloid, waxy, or lardaceous kidney is one in which the vascular walls, and especially those of the Malpighian coil, have undergone a complete albuminoid or amyloid metamorphosis. Here also the afferent vessel of the tuft has its walls thickened and its lumen increased in diameter. As a rule, the walls of the blood-vessels are the only part of the organ attacked.

It is usually preceded or accompanied by a similar metamorphosis of the liver, spleen, and intestinal tract.

This form of lesion is rare. Kidneys are often thought to be waxy, but they seldom show any reaction when put to the test.

Etiology.—The ascribed causes are long-continued suppuration, especially in connection with bone and joint lesions, also phthisis, empyæma, pyelitis, syphilis, ague, and any obscure cachexia.

It is an open question, however, whether this hyaline or waxy change ever occurs independently of a syphilitic taint; for it not infrequently happens that necropsies, made in connection with suppurating bone diseases which have lasted many years, show no waxy change, while a short period of suppuration in connection with syphilis will reveal an extensive waxy transformation in one or more organs.

From these clinical and pathological facts it seems reasonable to consider the syphilitic taint in connection with a suppurative process absolutely essential for the production of this hyaline or waxy metamorphosis.

This change in the vascular walls may occur in connection with any of the chronic forms already enumerated, and consequently is no more a separate and distinct renal lesion than the gouty variety; but usually it is the passive metamorphosis which is associated with the amyloid

transformation, and the organs grow larger, and are, as a rule, dark
in color from the albuminoid metamorphosis.

Macroscopic Anatomy.—Usually the kidneys are enlarged and dark
in color. Their capsules are normal and non-adherent to the under-
lying renal surface, which, after enucleation, is found to be perfectly
smooth, unless this change has been superinduced upon a chronic
form of diffuse nephritis.

The cortex is thickened, and the pyramids of Malpighi are dark
and distinct. The Malpighian bodies are also quite dark and promi-
nent, usually about the size of millet-seeds.
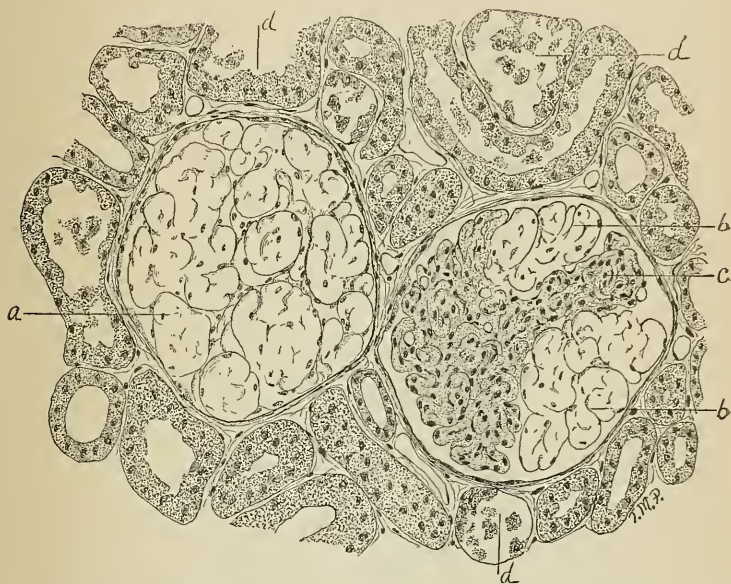
FIG. 24.—WAXY DEGENERATION OF BLOOD-VESSELS OF GLOMERULUS. × 350 and reduced.

a, The tuft is completely transformed into a waxy mass; *b,* portions of vascular loops, waxy;
c, vascular loops in normal condition; *d,* convoluted tubules with swollen, degenerated, and
peeling epithelium. (Delafield and Prudden's "Handbook of Pathological Anatomy and
Histology.")

Microscopic Anatomy.—The walls of the small vessels of the tufts,
and small arterioles outside the tufts, are infiltrated with a substance
called albuminoid material; a change which may involve all the
vessels of the kidneys. The afferent vessels are thickened and
expanded by this amyloid change in their walls. The thickening
and dilatation are quite marked even early in the development,
and become more and more marked as the disease becomes more

advanced. Later there may be some increase in the interstitial tissue, followed by a fatty infiltration of the epithelial corpuscles. This condition may be developed in conjunction with a chronic diffuse nephritis; in such instances the change is more complex, and the symptoms are dependent upon the predominating lesion.

The macroscopic test for amyloid or waxy transformation is a change in color upon the addition of a solution of iodine to the cut surface of the organ. If this waxy condition has occurred, those portions which are the seat of the amyloid change will turn a dark mahogany color when the iodine solution comes in contact with the affected portion.

The most delicate test for microscopic examination is the methyl-green, originally described by Curschman.[1]
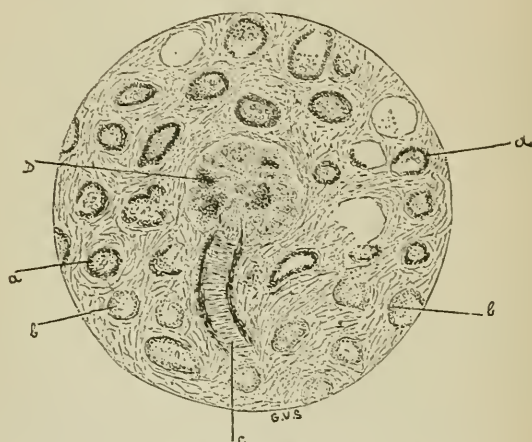

Fig. 25.—Early Stage of Waxy Metamorphosis of the Kidneys, Stained with Methyl-Green. × 350.

a, Transverse section of blood-vessels showing a thickened wall and expanded 'lumen; *b*, uriniferous tubule not affected by amyloid change; *c*, afferent vessel of Malpighian tuft with thickened walls and expanded lumen from waxy change; *d*, Malpighian tuft showing partial waxy metamorphosis. The darker rings indicate the waxy charge.

It is best applied as follows: the specimens are soaked for several hours in a two-per-cent aqueous solution of methyl-green, then washed in water until the deep-green color commences to assume a decided rose tint; they are then mounted in equal parts of glycerin and water.

When examined microscopically, this rose color, indicative of the seat of the amyloid change, is found to be confined to the walls of the smaller vessels and those of the Malpighian coil; the intervascular

[1] Curschman, Archiv f. Path. Anat., lxxix., iii., 1880.

portion or parenchyma remaining green and free from any waxy transformation.

Symptoms.—These are not marked, and are usually inseparable from those accompanying the exhausting processes in general. Late in the disease, cephalic symptoms may present themselves in the form of a slight wandering of the mental faculties, sometimes reaching to a mild delirium. There is usually diarrhœa, but this is not always marked, unless the vessels of the intestine have undergone the same change as those of the kidneys. There is almost always enlargement of the liver and spleen, but œdema is seldom present, and even then only to a slight degree.

In all the diseases of the kidneys, the œdema is, in a large measure, directly dependent upon the quantity of water discharged from the body; consequently, when the quantity of urine voided is large, the œdema is slight; but when small, the reverse is true, and general anasarca is frequently developed.

Diagnosis.—The quantity of urine voided daily is very large, and the specific gravity unusually low, ranging between 1.005 and 1.001. A trace of albumin and hyaline casts may occasionally be found, but both are rare.

The previous history and the very low specific gravity are the diagnostic points of the disease.

Prognosis and Treatment.—There is little or no hope for recovery, unless the cause can be removed; if this can be effected, the kidneys will probably return to their normal condition. This, however, is a hard question to decide, as we have no way of confirming the accuracy of our diagnosis if the patient survives. The prognosis nevertheless rests upon the primary disease, and not upon the renal lesion. The treatment also refers entirely to the primary disease; an improvement in that will of necessity retard the renal lesion, and tend to establish a more normal condition of the kidneys.

If, on the other hand, the syphilitic taint be the chief and determining cause, a strict anti-syphilitic line of treatment should be insisted upon, and the number of amyloid kidneys met with will then be less frequent.

Summary.—The foregoing classification of renal lesions is not wholly new, but its modification and presentation in this concise pathological and clinical form is the result of a careful study of a large number of clinical cases, and the pathological data furnished by several hundred necropsies.

Each lesion is believed to be separate and distinct from the com-

mencement; there is not first a parenchymatous enlargement, followed
by a contraction or cirrhotic stage, as formerly taught.

The chronic parenchymatous group may need a word of explana-
tion, as it resembles the chronic diffuse variety in some respects, but
a careful analysis of the clinical and urinary symptoms, as well as the
microscopic changes, clearly establishes its identity as a separate and
distinct class.   A long-continued lesion of the epithelial cells must,
of necessity, produce some change in the intertubular tissue, but from
the method of its production, and the fact that the major part of the
lesion is primarily in the epithelial cells, and not of inflammatory
origin, it is established as a separate and distinct group.   It has been
frequently, but wrongfully, classed as a diffuse lesion.

The same holds true in reference to the sclerotic type, for the
primary lesion originates in and is principally confined to the inter-
tubular tissue, while the epithelial cells suffer a slight change, but
yet this should not be classed as a diffuse lesion.

By an observation of the principles laid down for each, repre-
sentative cases have been repeatedly diagnosticated at the bedside,
and in over a hundred consecutive cases, the necropsy has con-
firmed the diagnosis.   Most of the drawings illustrating the different
lesions are from sections made from these cases.

By some, chronic congestion would be included in the class com-
monly called Bright's; but it is here omitted, as it is generally con-
ceded that it does not give rise to albumin and casts until structural
changes have been developed in the epithelial cells or intertubular
tissue, or both; then we have one of the lesions already enumerated.
In this light the chronic congestion becomes a cause of renal disease,
and in no sense an intrinsic kidney lesion.

This arrangement in part duplicates some of the lesions, but from
their clinical differences, they appear to deserve this distinct multi-
plicity.

This classification is based upon the more recent theory that the
kidney progressively enlarges or decreases in size from the inception
of the disease until its termination, and not upon the old idea of pro-
gressive enlargement followed by progressive diminution in size.   A
careful study of the clinical symptoms in connection with the necropsy
findings clearly demonstrates the identity of each of these varieties.
This classification is based upon the study of several hundred post-
mortem examinations, in which more than one hundred had one of
the active forms.

It should always be remembered that the exact kind of lesion can-

not be determined by one analysis or a single sign or symptom, but only by an accurate appreciation of the causation and method of production, together with an analytic study of the clinical history and the sum total of the results of several examinations of the urine. When this is accomplished, the exact variety can be determined with a wonderful degree of precision, and the size and the exact condition of the kidneys predicted with an astonishing accuracy.

For the large number of distinct renal lesions that can be recognized during life, as well as at the necropsy, the term Bright's disease no longer seems appropriate; but if it is desirable in honor of the discoverer to still retain his name, it would be better, as Prof. Andrew H. Smith and others have suggested, to speak of the class as Bright's diseases, as there is no longer a Bright's disease.

By this arrangement it is quite evident that the quantity of albumin discharged with the urine, in renal lesions proper, bears a direct relation to the amount of retrograde change in the epithelial protoplasm. When this epithelial metamorphosis is slight, the quantity of albumin is small; but when the epithelium is extensively implicated, its amount is large. Although the physiologists teach that albumin makes its escape through the vascular walls of the Malpighian coil, its transudation in connection with the renal diseases appears to be directly dependent upon the integrity of the epithelial cells. When the epithelial metamorphosis is extensive, there is a large amount of effete material retained in the blood, which, together with the cause of the kidney disease, greatly impairs the nutrition of the wall of the vessel composing the Malpighian tuft. It loses its power to hold the serum albumin within its lumen, and it is forced through into the uriniferous tubule with the water. With a slight retrograde change, less effete material is retained, the walls of the blood-vessels retain a higher degree of integrity, and prevent so large an escape of albumin.

The quantity of urine discharged also is in direct relation to the change in the afferent vessels of the Malpighian coil; for in every lesion where this afferent vessel of the Malpighian coil has a thickened wall and an expanded lumen, the quantity of water discharged is constantly large, but in all those lesions in which the afferent vessel remains unaffected, the quantity of urine discharged is invariably normal or more often perceptibly diminished. The diabetic parenchymatous metamorphosis will be discussed in detail in the chapter devoted to that disease.

COMPARATIVE TABLE SHOWING CHANGES IN THE URINE, WITH THE TWELVE DIFFERENT LESIONS.

BRIGHT'S DISEASES.	CHEMICAL EXAMINATION.				MICROSCOPIC EXAMINATION.
VARIETY OF RENAL LESION.	COLOR.	QUANTITY.	SPECIFIC GRAVITY.	AMT. OF ALBUMIN.	THIS REFERS TO BLOOD AND CASTS ONLY.
1. Acute Parenchymatous Metamorphosis of the Kidney.	Abnormally High.	Very Small.	High, from 1.017 to 1.030.	Abundant.	Early: Hyaline, epithelial, nucleated, and finely granular; small in diameter, and abundant. Later: Some coarsely granular and fatty, with large diameter.
2. Chronic Parenchymatous Metamorphosis of the Kidney.	Abnormally High.	Very Small.	High, from 1.015 to 1.030.	Abundant.	Large hyaline, coarsely granular, and fatty casts, and large amount of cast debris.
3. Parenchymatous Metamorphosis of the Kidney with Pregnancy.	Variable.	Variable, but usually Small.	Variable.	Variable, Trace to Abundance.	All varieties of casts may be met with, even blood casts from the renal obstruction. Early it will resemble No. 1, later No. 2.
4. Parenchymatous Metamorphosis of the Kidney with Diabetes Mellitus.	Lemon-yellow, but later Pale.	First Large, then Small or Suppressed.	First High, 1.025 to 1.060; late, Low; or at last Lower.	At first Glucose; later, trace of albumin.	None until late in the diabetes, when hyaline and fatty casts appear, occasionally a few granular.
5. Parenchymatous Infiltration Metamorphosis of the Kidney with wasting Diseases.	Normal or Watery.	Normal.	Normal.	None.	Examination negative.
6. Acute Diffuse Nephritis.	Abnormally High, Smoky, or Bloody.	Very Small or Suppressed.	Low, 1.020 to 1.012.	Abundant, also blood.	Blood and blood casts, a diagnostic feature. Early: Small, hyaline, epithelial, nucleated, finely and coarsely granular, in abundance. Later, fatty and larger casts.
7. Chronic Diffuse Nephritis—Large Kidney.	Peculiar Pale.	Constantly Varying; sometimes Small, then Large.	Low, 1.017 to 1.010.	Constantly Varying from None to Abundance.	The quantity and variety of casts is constantly varying, at times abundant, and at others absent. The constant fluctuation is diagnostic. All varieties may be found during its course.
8. Chronic Diffuse Nephritis—Small Kidney, Hyaline Thickening of the Afferent Vessels.	Peculiar Pale.	Usually Large, 80 to 100 oz. a day.	Low, 1.010 or Lower.	Abundant and Continuous.	As a rule, no casts are found; but occasionally a hyaline or fatty cast may be detected.
9. Chronic Diffuse Nephritis—Small Kidney, without Vascular Thickening.	Peculiar Pale.	Always below Normal; Small.	High, 1.015 to 1.025.	Usually Abundant and Continuous.	Hyaline, epithelial, nucleated, finely and coarsely granular, and fatty casts, of all sizes, and in abundance continually. Blood and blood casts occasionally found.
10. Interstitial Nephritis or Cirrhotic Kidney; Cirrhotic, Sclerotic, or Red Atrophy; Thickening of Afferent Vessels.	Nearly like Water.	Very Large.	Low, 1.010 to 1.005.	Usually Absent, occasionally a Trace.	As a rule, no casts are found; but occasionally a hyaline cast is discovered.
11. Gouty Kidney.	Nearly like Water.	Very Large.	Low, 1.010 to 1.005.	Absent or a Trace.	
12. Waxy, Amyloid, or Albuminoid Transformation of the Kidney.	Nearly like Water.	Exceedingly Large.	Low, 1.005 to 1.000 or Lower.	Usually absent, occasionally a Trace.	

CHAPTER VII.

RENAL HEMORRHAGE. HÆMATOGLOBINURIA. ANÆMIA.

RENAL HEMORRHAGE.

Hemorrhage from the kidneys cannot be classed as a distinct disease, dependent, as it is, upon so many other renal affections which usually have marked symptoms of their own. But it is often desirable, especially in medico-legal cases, to differentiate between it and hemorrhage from other parts of the genito-urinary tract.

Etiology.—The causes of renal hemorrhage are quite numerous. They are cancer, sarcoma, tubercle of the glands, suppurative nephritis, irritation of crystals, acute diffuse nephritis, purpura hemorrhagica, scorbutus, scurvy, pernicious anæmia, leucocythæmia, eruptive fevers, yellow-fever, phthisis, parasites, acute and chronic congestion, injury with or without rupture of the renal substance, embolism and thrombosis of the renal vessels, and infarctions. Overdoses, and sometimes even large doses, of certain medicines such as turpentine, cantharides, squills, and all forms of irritating diuretics, are liable to produce this result.

Pathological Anatomy and Symptoms.— No pathological changes are developed in the kidneys which cannot be referred to the exciting or irritating agent. Under the microscope, blood will be found in the uriniferous tubules, and the blood-vessels will be congested. The changes due to whatever disease it may complicate will also be observed.

The *symptoms* also are those of the cause, and previous to death the urinary manifestations only can be relied upon for a positive diagnosis. The *urine* is red in color, the density of the shade depending upon the quantity of blood contained. The reaction is usually alkaline; albumin is present, and the specific gravity is high.

When examined by the *microscope*, varying quantities of blood-corpuscles and blood-casts are present. All of these symptoms, except the presence of blood-casts, may appear in the urine without the hemorrhage being necessarily renal in origin. But if blood-casts are found, and especially if numerous, some of the blood at least can be positively asserted to have come from the kidneys. Nephritic

hemorrhage, on the other hand, may also occur, and blood-casts be absent in the urine; in such a case, a positive diagnosis is impossible. Therefore, in a medico-legal case, it would be impossible to say that the blood did not come from the kidneys, in the absence of these blood casts. But when blood-casts are found in the urine, a positive assertion regarding the source of the blood can be made.

Prognosis.—In itself this affection is not serious, but it always renders the prognosis of the exciting disease or injury more unfavorable.

Treatment.—Little or nothing can be done in the way of treatment, except that which may be indicated by the cause. Ergot in small and repeated doses is of service, if not contra-indicated by some other condition. The same is true of gallic acid; this, however, is liable to produce temporary retention, which is always an objection to its use as an internal hemostatic.

The hemorrhage, however, except in traumatic injuries, is rarely of sufficient importance by itself to necessitate any special or independent treatment.

HÆMOGLOBINURIA.

Definition.—Hæmoglobinuria is a condition in which dark-colored urine which contains hæmoglobin, with but few, if any, blood-corpuscles, is excreted by the kidneys. There may be only one attack, or there may be several which follow one another with a certain degree of regularity. It is then known as periodic hæmoglobinuria.

Etiology.—This is still a mooted question. This kind of urine has been met with in connection with a number of dissimilar conditions, which naturally renders its actual causation extremely doubtful. It has made its appearance after muscular exertion, as recorded in the case of soldiers after a prolonged march, and occasionally after other forms of muscular fatigue; after mental excitement in connection with, or as a sequel to, various diseased conditions, viz.: malaria, syphilis, rheumatism, malignant and septic fevers, putrid and typhus fever, purpura, scurvy, phthisis, etc. After the use of, or poisoning by, naphthol, pyrogallic acid, arseniuretted hydrogen, carbon anhydride, chlorate of potassium, etc. The precise relation of cold as a causative agent is yet uncertain, although there is considerable proof in favor of its acting as a secondary excitant, if not as a direct cause.

The theory of Ponfick appears quite rational,[1] viz., that a condition of hæmoglobinuria is produced by or is attributable to a destruc-

[1] Berliner Klinische Wochenschrift, No. 26, 1883.

tion of the red blood-discs; that this condition is divisible into three forms, dependent upon intensity and in which the corpuscular débris is disposed of in as many different ways. In the *first* or mildest form, the detritus accumulates in the spleen, which causes an enlargement of that organ.

In the *second* or intermediate degree, the liver secretes an excessive quantity of bile (hypercholia), and in this way relieves the system.

In the *third* or severest form, the corpuscular débris is excreted from the plasma of the blood by the epithelium of the kidneys, and gives rise to the condition known as hæmoglobinuria.

The enumerated causes certainly point in this direction.

If this theory be true, it offers a very rational and satisfactory explanation for the unusually high-colored urine in pneumonia and the severe forms of blood diseases. It would appear, therefore, that a partial hæmoglobinuria, resulting from the destruction of the red blood-discs, is the true explanation of the high-colored urine.

The hepatic portion of this theory also affords a tangible reason for the icterus in this class of diseases.

The splenic portion of the theory explains the universal enlargement and the metamorphotic changes so generally met with in connection with that organ.

The renal portion explains the development of this peculiar urine, and accounts for the precise changes in color with every fluctuation of the acute diseases.

Pathological Anatomy.—The necropsies that have been made upon persons who have died, during an attack of acute or periodic hæmoglobinuria, have been so few that nothing positive has been determined concerning this condition. If the above assumptions be true, little would be expected in the way of change in the organs. We would naturally expect to find a parenchymatous transformation in the glandular organs, and this may be one grand cause in producing these changes. It is certainly reasonable to believe that destruction of the red blood-corpuscles takes place in some part of the body, and that this destruction, in quite a number, if not in the majority, of the cases, is directly excited or influenced in some way by undue exposure to cold.

It has been suggested that there must be a condition of the nervous mechanism, by which it either does not permit of a healthy formation of the red corpuscles, or is so markedly sensitive that it affects these elements of the blood.

The very fact that certain chemical and medicinal agents, when brought in contact with the blood-discs, rapidly decompose them,

and the association of this disease or change in the urine with many of the acute blood diseases, points strongly to some blood poison, whatever it may be, as the agent which excites the destruction of the red blood-corpuscles and causes the appearance of the hæmoglobin in the urine. The observations of Boas and others make it possible that the destruction of the red blood-discs takes place in those parts of the body which are most exposed to the severe action of these elements. The whole subject, however, aside from its occurrence, is somewhat in a state of uncertainty.

Symptoms.—The attacks may not be paroxysmal, but in the majority of instances they are; hence the name paroxysmal hæmoglobin-uria. They begin with a slight chill or shivering sensation, followed by a rise in temperature, which in one recorded case rose to 103° F., or 39.4° C.; and in another to 104° F., or 40° C. As the paroxysm subsides, the temperature falls, and in this respect it simulates the malarial diseases. The urine voided during the attack, or early in its subsidence, is found to contain albumin; a little later, the urine passed is dark in color, resembling port wine, or even of a deeper hue. At the end of a few hours it will have returned to its normal color and composition. In other cases, this peculiar urine persists for several days, or even weeks.

Microscopical Examination.—Very little that is abnormal is found in some, a few blood-corpuscles are detected; while in other samples, they are entirely absent. Occasionally, a few hyaline casts may be found, but their occurrence is exceedingly uncommon. By a spectro-scopic analysis of the urine, every evidence of hæmoglobin will be found. This, however, is not a practical test for the general practi-tioner.

Its presence may also be ascertained by Heller's or the guaiac test, see section on blood.

In some of the recorded cases, there has been a recurrence of these attacks at varying intervals for a long period. In one, the patient was closely observed for several years. He was subjected to cold foot baths, which invariably and quite rapidly brought on a recurrence of the symptoms. These urinary changes have been thought to take the place of a malarial chill.

Only one case in which the symptoms in any way approached this condition has been directly observed, but opportunities have offered for the examination of several samples of the urine from such patients. In the instance cited, the urine looked bloody; but compared with its color and general microscopic appearances, it contained so few of the

red blood-discs, that practically it might be said that there were none present.

Several times the question has been asked: "How would you account for black urine, without any other symptoms resembling a malarial attack, in persons suffering previously from malaria, and in whom the voiding of this kind of urine appeared to replace one of the paroxysms?"

This query has most frequently come from physicians practising in decidedly malarial sections of the country and they must have been instances of hæmoglobinuria.

As a spectrum analysis is not very convenient or practical, and the chemical tests are somewhat uncertain, the examination is often negative.

Satisfactory methods for the detection of hæmoglobin cannot always be instituted to confirm the diagnosis. But the sudden discharge of such dark urine, and an absence of the red blood-corpuscles when examined microscopically, would warrant the diagnosis of this trouble. Carbolic-acid poisoning occasionally causes the discharge of black or very dark urine, but the two could hardly be confounded. It is possible that the dark urine of carbolic-acid poisoning is only a form of hæmoglobinuria produced by the action of this acid.

Prognosis.—So far as this symptom is concerned, there appears to be no immediate danger, as very few cases are recorded in which the patient died at the time of the attack.

Treatment.—This depends largely upon the pre-existing condition. If traceable to a malarial origin, quinine or some of the cinchona alkaloids, as in all miasmatic affections, will yield the best results. When attributed to a syphilitic taint, the combined use of mercury and the iodide of potassium offers the best prospect of recovery, and naturally tends to prevent recurrence.

In connection with the acute blood diseases, no special treatment is called for, further than that of the general disease with which it is associated. When there is a tendency to recurring attacks, all exposure to cold and sudden changes in temperature *must* be avoided. Warm woollens must be worn next to the skin, and this is especially true with regard to the winter season. The general nutrition should be improved by chalybeates, tonics, good food, and pure air.

ANÆMIA OF THE KIDNEYS.

Definition.—This is a condition of the kidneys in which the organs are found to be extremely pale, and the vascular areas devoid of blood.

Etiology.—This abnormality is caused by pernicious anemia, purpura hæmorrhagica, leucocythæmia, excessive hæmorrhage either external or internal, and with wasting diseases in general.

Macroscopic Anatomy.—The kidneys remain about normal in size. The principal change is the extreme pallor, both of the cortical and the medullary portion.

Microscopic examination shows the capillaries free from blood and empty, and the epithelial cells are pale and granular.

Symptoms.—There are none specially referable to the kidneys, but those of the condition with which it occurs.

Its *treatment* is that of the condition by which it is produced.

CHAPTER VIII.

ACUTE CONGESTION. CHRONIC CONGESTION.

ACUTE HYPERÆMIA OF THE KIDNEYS.

DETERMINATION OF BLOOD TO, OR ACUTE CONGESTION OF THE KIDNEYS.

Definition.—Hyperæmia of the renal glands may be due to the determination of more blood to the kidneys than the normal quantity, or it may be due to a temporary obstruction which prevents the venous return.

In the variety which is commonly called acute congestion, there is an abnormal influx of arterial blood, and a consequent dilatation of the arterial capillaries from the cardiac side.

Etiology.—Acute congestion may be caused by irritation or paralysis of the vaso-motor nerves, by acute inflammation of the kidneys; the blood-poisoning of various diseases, as in scarlet fever, small-pox, measles, etc. (if a marked parenchymatous metamorphosis is not developed), or by a diffuse nephritis; exposure to cold, and in malarial attacks. With the last, congestion is very marked in the kidneys as well as in the other visceral organs. It is also produced by irritating diuretics, such as cubebs, copaiba, turpentine, cantharides, potassium nitrate, etc., and by carbolic-acid poisoning. Digitalis practically produces acute hyperæmia, like cold, by increasing the general systemic and diminishing the renal tension, and in this way an increased volume of blood is forced upon the kidneys. This is the true explanation for the diuretic action of digitalis. But it only acts well when there is slight obstruction in the intertubular plexus. Concerning *vaso-motor* paralysis as a cause, its exact modus operandi is not clearly explained; but with the high arterial tension of the general arterioles outside of the splanchnic arcade, there appears to be a corresponding dilatation of the renal arterioles, and certain drugs appear to cause a dilatation of the splanchnic arcade and not of the arterioles in general. *Diabetes insipidus* and *polyuria* are both instances associated with renal *vaso-motor paralysis.*

Pathological Anatomy. Macroscopic Appearances.—The kidneys are normal in size, or slightly enlarged; their capsules are not thickened nor adherent to the underlying renal suface, which is smooth and dark in color. The cut surfaces also are darker than normal. The epithelial cells of the cortex and pyramids are unchanged, except in color, which is deepened. The renal substance is abnormally soft, and the vessels are engorged with blood. Throughout the cortex dark-red points are plainly visible to the unaided eye, and represent the location of congested Malpighian tufts. Bloody serum often exudes from the incisions made in its substance.

FIG. 26.—ACUTE RENAL CONGESTION WITH INFARCTIONS.

A, Pyramidal portion deeply congested; *B*, cortical portion deeply congested; *a*, occluded vessels; *b*, Malpighian corpuscle congested.

Microscopic examination shows the blood-vessels to be distended with blood, which is principally located in the arterial side and in the capillary loops of the glomerulus, the walls of which, in some instances, have given way and permitted of small extravasations within Bowman's capsule, the effused blood passing into the uriniferous tubules. Extravasations may also occur from the small vessels before the tufts are reached, but this is the exception. Occasionally a tubule may be found that is packed full of red blood-corpuscles for a considerable distance, or they may contain hyaline plugs or casts. All these changes

are sometimes present in a single field. Some of the epithelial cor-
puscles are a little opaque, but the change in their protoplasm is not
marked, and rarely reaches the condition known as cloudy swelling.

Ecchymotic spots are sometimes found in the pelves of the kidneys.

Symptoms.—The general or rational symptoms will be those of the
exciting disease rather than those which are directly referable to the
renal lesion proper. In that form traceable to cold or irritating
diuretics, the disease may be ushered in by a chill or strangury, great
pain in the loins and hypogastric region, and some febrile movement,
associated with or followed by almost, if not total, suppression. The
condition of the *urine* is the diagnostic element.   *Urinary Examina-
tion.*—The urine will be diminished in quantity, high colored, with an
increased specific gravity, and it will contain blood and albumin, or
both may be absent. Under the microscope, blood and blood-casts
and hyaline casts will usually be found; also, an abundance of the
urates. These symptoms may last for a few hours only, or be pro-
longed for several days and finally terminate in recovery, or degener-
ate into a more chronic form of renal lesion. The albumin in this
disease comes largely from the blood-corpuscles, or is forced through
by mechanical pressure. The presence of blood in the urine is not
diagnostic, for urine which does not contain blood-casts cannot be
said to come from the congested kidneys, however marked the other
symptoms may be. On the other hand, congestion, even with suppres-
sion, can and does occur, and neither blood nor albumin are found in
the urine; such cases are somewhat rare but severe when they do
occur. As the congestion subsides, the first urine passed will be
heavily loaded with urates, but does not contain albumin or casts.

Prognosis.—In this form the congestion usually subsides sponta-
neously, the prognosis being almost always favorable. There are,
however, instances, especially those produced by malarial poisoning
or some irritating diuretic, in which the functions of the kidneys are
entirely arrested, and if not speedily relieved, the patient will die
from suppression and the consequent uræmia.

Treatment.—This must be more or less vigorous, depending upon
the severity of the attack. In some cases, none will be necessary; in
others, rest in bed will be all that is required. Dry or wet cups should
be applied to the loins, to be followed by a warm poultice. A drastic
cathartic is always in order, ten or twenty grains (0.6 gram, 1.4
gram) each of calomel and jalap is one of the best. If a relia-
ble preparation of elaterium can be obtained, it is better than the cal-
omel and jalap. It should be used in one-eighth grain (0.008 gram)
doses, every fifteen or twenty minutes, until three-fourths of a grain

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(0.048 gram) have been given, or the intestines have commenced to move. After the attack has reached its height, and there is a fall in the blood tension, digitalis is to be used freely, and in full doses. As there is apt to be nausea or vomiting, and difficulty in retaining any-thing in the stomach, the tincture will be found the most reliable. This preparation may be given in ten minim (0.6 c.c.) doses every three hours, until the renal secretion is started, and then less fre-quently.

In cases threatened with uræmic convulsions and coma, a full dose of pilocarpine, administered hypodermatically, will be necessary to prevent impending death. By a judicious administration of these medicinal agents, a case of uncomplicated renal congestion will sel-dom prove fatal; but, if superimposed upon a chronic kidney disease, the best directed remedies will many times prove inadequate.

HYPERÆMIA OF THE KIDNEYS.

PASSIVE OR CHRONIC CONGESTION OF THE KIDNEYS.

Definition.—Hyperæmia of the kidneys is an active or passive con-dition, the latter having an acute or chronic character.

In the active, there is an abnormal influx of arterial blood to, and a consequent dilatation of, the arterial capillaries ; but in the passive congestion, there is some obstruction to the venous current, which prevents the normal escape of blood from the kidneys, and causes an engorgement of the renal veins.

Etiology.—This lesion is purely mechanical in origin. It is often due to some lesion of the heart, especially pulmonary insufficiency, mitral stenosis or regurgitation, more often the latter, fatty degene-ration and dilatation or endocarditis—in fact, all conditions in which there is an interference with the cardiac and pulmonary circulation, which forces the blood back upon the general venous circulation. Occasionally it is associated with adhesive pericarditis, or an exten-sive hydropericardium. The following diseases of the lungs will produce it, viz., emphysema, chronic interstitial pneumonia, pleurisy with effusion, also aneurisms of the aorta, and tumors of the medias-tinal spaces or abdominal cavity, which press upon the inferior vena cava above the renal veins. Tumors pressing upon the pulmonary veins act in like manner.

The gravid uterus is another cause of a temporary form of chronic congestion of the veins of the kidneys.

Thrombosis of the inferior vena cava or renal veins may be included among the causes.

Pathological Anatomy. Macroscopic Appearances.—In this, the chronic form, the kidneys may be smaller, of the ordinary dimensions, or considerably larger than normal, the latter being the rule. A peculiar feature is their extreme hardness, which has been called a "stony hardness." The capsules of the organs are about normal in thickness, and non-adherent to the underlying renal tissue, which is usually quite smooth after enucleation.

It may occasionally appear lobulated, but this is due to remnants of the fœtal lobules becoming more apparent by the congestion and enlargment. The stellar veins of Verheyen are remarkably prominent. The cut surfaces have a succulent appearance, but in reality are quite firm. Both the cortical and medullary portions are dark in color, and this is more marked in the pyramids than the labyrinth; the markings of the latter are sharply defined and straight. The Malpighian bodies are quite prominent, but not so decided as in the acute form.

Microscopic Examination.—The veins are found under the microscope to be very much congested, but now the engorgement is most marked in the large veins and interlobular plexuses, the tufts and arterial capillaries being comparatively free. The epithelial cells of the tubules are moderately swollen, opaque, approaching toward a granular transformation, and by their enlargement often diminish the lumen of the tubules both in the medullary and cortical portions. This change is most easily recognized in the straight and collecting tubules as a distinct lesion; the lumen often contains hyaline plugs resembling casts. This cast-like substance is seldom, if ever, found in the convoluted tubules. There does not appear to be any inflammatory new formation in the interstitial tissue, but the change appears to be a nutritive one, by which more material has been brought to the organ than is absolutely required. As a consequence, the substance of the glands absorbs these nutritive elements in abnormally large quantities and hypertrophies, without the intervention of any truly inflammatory process. An inflammatory action may at any time be engrafted upon this lesion. This is more likely to be the case than if the organs were normal. Bowman's capsule, and in fact every part, may be thickened. This condition has been considered as one form of that large list usually classed under the common term Bright's. But, as already stated, it is, more strictly speaking, a direct cause of the renal lesion.

Symptoms.—Aside from the urinary indications, there are no definite characteristics by which this disease can be diagnosticated. Such cases present a large variety of symptoms, all of which, however, are directly traceable to the pre-existing lesion, which is producing

the kidney trouble. Associated with these we find positive alterations in the urine, which readily indicate the true nature of the disease.

Diagnosis.—With chronic obstruction to the venous return, the œdema will first appear in the lower extremities, and gradually work up to the large serous cavities and superior extremities; while in primary renal disease the œdema is first noticed under the eyes, and later in the extremities.

Urinary Changes.—With chronic congestion we find the urine very much diminished in quantity, with a high specific gravity, 1.025 to 1.030 or higher; of a very dark color and often heavily loaded with urates. Albumin and blood-corpuscles are quite common, and occasionally blood-casts are present. The quantity of albumin is usually small, and this may be accounted for in two ways. It may be due to an incomplete metabolism of the proteids, and a filtration of the undigested albuminates, and to mechanical pressure which is very greatly increased by the venous obstruction; as the pressure rises and the metamorphotic changes in the epithelium become more extensive, the amount of albumin in the urine increases. Casts are infrequent, but occasionally a small hyaline, a finely granular, or blood-cast, may be present; still more rarely a fatty cast can be added to the list. The blood-cast, however, is the only variety which is positive evidence that the blood originated in the kidneys. The diminution in the quantity of urine will progressively grow less until a condition, similar to acute suppression, is developed. This will often give rise to a uræmic attack, which, if not immediately relieved, will cause death either in convulsions or coma.

The kidneys, thus constantly impaired, are quite likely upon the slightest provocation to become the seat of a more acute process. Necessarily, therefore, excesses in eating or drinking, severe attacks of indigestion, or a sudden yet moderate exposure to cold, will often excite an acute congestion or inflammation of the renal glands. In this way, the acute exacerbations which frequently occur, and in which there is a discharge of bloody urine, are explained. The urine will now be small in quantity, highly albuminous, and contain epithelial and blood-casts, often in abundance. Exacerbations occur frequently, until finally they prove fatal. During the remissions, the casts will entirely disappear, and often only a trace of albumin continues, but the quantity of urine usually remains small, high colored, and of high specific gravity.

Prognosis.—Naturally this depends, *first,* upon the severity of the primary disease and the influence of treatment; *second,* upon the frequency and the severity of the acute exacerbations and the concurrent

renal lesions. Death seldom results from the effects of this disease simply, but is caused by one or more complicating influences.

Treatment.—In determination of blood to the kidneys, the treatment required is often quite active, but in the passive or obstructive variety the reverse is true. All medicinal agents which tend to improve the pre-existing disease will improve the condition of the kidneys. If the renal congestion be dependent upon an irreparable damage to the heart or pulmonary organs, or to a tumor pressing upon the veins which cannot be removed, little or no relief can be expected from internal medication. Unless the cause can be removed, the congested condition of the kidneys must remain.

Digitalis is not called for, but contra-indicated, as it tends to increase the pressure upon the tuft of vessels constituting the glomeruli. It will, undoubtedly, cause an increase in the quantity of water discharged, but it does not overcome the venous engorgement. On the other hand, it tends to increase the congestion, and diminishes the excretory and nutritive power of the renal glands.

The sending of more blood to the kidneys must be guarded against, and a free escape favored in every possible way. This is best accomplished by acting upon the bowels and skin, with a few dry cups applied to the loins, and followed by a warm poultice.

As a rule, most of the diuretics are theoretically contra-indicated, and in most instances have proven themselves practically of no avail.

Jalap, calomel, and elaterium are often serviceable. Small doses of pilocarpine frequently administered are also useful.

In the acute stage of an exacerbation, the treatment must be active; prompt catharsis and diaphoresis will often relieve the symptoms and prolong life.

CHAPTER IX.

PYELO-NEPHRITIS. PYELITIS. PYONEPHROSIS.

PYELO-NEPHRITIS.

SUPPURATIVE NEPHRITIS. SURGICAL KIDNEYS.

Definition.—This is an intense inflammatory condition of the kidneys, terminating in the formation of pus, which may be localized or diffused throughout the substance of the organs. The term surgical kidney is especially applicable to this lesion when it is directly traceable to a surgical operation, as is often the case. In fact, it is one of the "bugbears" of genito-urinary surgery.

Etiology.—The causes of pyelo-nephritis are, injuries, deposition of crystals in the uriniferous tubules or pelves of the kidneys; renal parasites, renal calculi, pyelitis, lodgment of calculi in the ureters, cystitis, cystic calculi, tumors obstructing the ureters or neck of the bladder, enlarged prostate, prostatic calculi, inflammations and abscess, urethral calculi and strictures, and all operations upon the genito-urinary tract, gonorrhœa, urethral chancres and chancroids, pyæmia and septicæmia; it also occurs in connection with paraplegia and hemiplegia. The more common, however, are cystitis, alone or associated with calculi, stricture of the urethra, enlarged prostate, operations upon the genito-urinary tract, and gonorrhœa.

Pathological Anatomy.—This lesion, for convenience of description, will be divided into three stages. In the *first* or early development, the kidneys, to all outward appearances, are simply congested. This is, however, more marked than in an ordinary and simple congestion. When the organs are laid open, the mucous membrane of their renal pelves is congested and covered with mucus and little patches of a fibro-plastic exudation, which are adherent to the membrane. This condition has been described as a diptheritic pyelitis.

When such kidneys are examined under the microscope in thin sections, lymphoid corpuscles will be found quite abundant between the tubules, but usually localized in small foci; the intervening tubules remaining nearly normal, while in places minute abscesses are

found. But as the disease progresses to what may be termed its *second* stage, and the one most frequently seen at the necropsy, the surface is studded with clumps of white points, varying in size from a pin's head to a walnut. These larger spots look like abscesses just underneath the renal capsule. Upon cutting into one, it is found to consist of purulent matter. These little abscesses are scattered all through the kidneys, but are usually more abundant in the cortical portion and near the surface.

Upon *microscopic examination*, what was an inflammatory focus in the previous stage, has developed into a localized purulent centre, which has no limiting wall of fibro-plastic material.

The tubules lying in the continuity of these abscesses have been
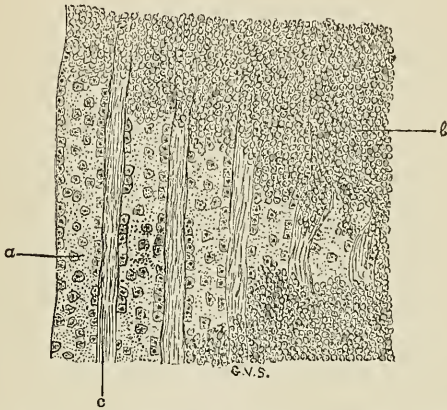
FIG. 27.—PYELO-NEPHRITIS OR SURGICAL KIDNEY. × 350.

a, Uriniferous tubule showing parenchymatous metamorphosis; *b*, diffuse suppurative zone; *c*, œdematous intertubular tissue.

liquefied and destroyed by the solvent power of the pus, so as to be completely cut across, and open abruptly on either margin of the abscess. The contents of one of these purulent centres are pus, granular detritus, and degenerating renal epithelium.

In still more advanced cases or the *third* stage, two or more of these purulent centres may have coalesced, until one-half or two-thirds, or even a whole kidney, may have become converted into a large sac of pus, having the capsule of the kidney for its limiting wall. Now the contents will be composed almost exclusively of pus, all evidence of the renal substance having been destroyed.

Associated with this condition and acting as a complication, there

is an inflammation of the bladder or ureter, most frequently the former.

It has been said that each purulent centre is due to the action of microbes, but as yet this has not been satisfactorily authenticated.

Symptoms.—In this peculiar lesion, the symptoms are exceedingly obscure, and naturally vary with, or are masked by, those of the lesion which causes the disease.

With any of the above-enumerated causes, a chill or a series of rigors may be developed. If due to a renal calculus, there may be severe pain, deep seated in the region of the kidneys. The urine may be unchanged, and the patient die at the end of a few days. When it follows a paraplegia, its occurrence is a little more clearly defined by the retention of the urine, its alkaline decomposition and cystitis, followed by the rigors.

In every instance, the chills are followed by some febrile movement with great depression, sweating, rapid and feeble pulse, hurried respiration, a dry and coated tongue, loss of flesh and strength, and a diminution in the quantity of urine voided. The patient falls rapidly into a typhoid state, and dies at the end of two or three days.

The *urinary* changes are very obscure, and do not give any signs upon which to base a diagnosis with any degree of certainty. The reason for this is, that the pre-existing condition in itself, often induces a diminution in the quantity of urine secreted, together with the appearance of pus and albumin. This lesion is not marked by the appearance of a large quantity of blood, and there is no discharge of characteristic casts.

A careful consideration of the producing lesion, and a close study of the clinical history and symptoms, will usually enable the examiner to surmise quite accurately, if not to positively diagnosticate this condition; and this supposition will frequently be confirmed at the necropsy.

Prognosis.—This lesion is of special interest in connection with surgical operations, as it is often developed just prior to, or is directly induced by the operation. In either instance the result is fatal. This is one of the great dangers in genito-urinary surgery and one which is unavoidable by the surgeon.

Treatment.—Perhaps the immediate performance of nephrotomy or nephrectomy would save the life of the patient in some few instances, but as the disease usually attacks both kidneys at the same time, the operation is not admissible from a practical standpoint. Further, the operation has not yet been proven to be a practically successful one, but on the contrary is rather losing favor. Evacuation

of the pus may be accomplished by aspiration, but so long as the cause remains, little or nohting can be accomplished. The only way by which any good can justly be expected is in the line of prevention.

The liability of this condition being developed as a sequel to the above-mentioned diseases should always be remembered, and steps taken to prevent the cause if possible. Considerable can be accomplished in this line, especially in connection with enlargement of the prostate gland, paraplegia, hemiplegia, etc. In these, the genito-urinary tract should be kept empty and clean, and in this way alkaline decomposition of the urine followed by a cystitis will be prevented, and the fatal issue retarded or avoided.

PYELITIS.

Definition.—Pyelitis is an inflammation of the pelves of the kidneys and of their calices. It may attack one or both organs at the same time.

Etiology.—Sometimes, though rarely, it occurs after exposure to cold, but its most frequent cause is the irritation of renal calculi in the pelves of the kidneys, or the presence of decomposing urine in the renal pelvis, due to some obstruction either in the urethra or bladder. Unduly acrid or acid urine may excite it. A mild form is sometimes excited by any of the varied forms of renal disease, and occasionally it occurs during pregnancy. It may also result from a cystitis, gonorrhœa, and all inflammatory conditions of the urinary tract by an extension of the inflammatory process. With gonorrhœa, the inflammatory process in the renal pelvis will suddenly develop, without any apparent involvement of the intervening portion of the urinary tract. Pyelitis may be excited by turpentine, cantharides, squills, and the many forms of irritating balsams, resins, etc., as well as by all acrid substances excreted by the kidneys.

A mild form of this disease is sometimes developed in the typhoid stage of cholera, in typhus fever, diphtheria, and all the exanthemata.

A hemorrhagic variety has been described, in which there is frequent and sometimes extensive hemorrhage into the renal pelvis. This condition occurs in connection with scurvy, purpura hæmorrhagica, pernicious anæmia, and leucocythæmia.

Pathological Anatomy.—The mucous membrane is very much congested and dotted with ecchymotic extravasations, and at places the epithelial surface is completely destroyed. In the most acute stage, there is little or no discharge, but as the disease advances and becomes

more chronic, a muco-purulent secretion is given off, and the membrane is relaxed and swollen. As the inflammation advances, the pelvis and infundibuli become enlarged and their walls thickened; the color of the mucous membrane changes to a grayish-white or slate color, and its surface is traversed by delicate capillaries. Should there be much mechanical irritation, ulceration is liable to be developed, which may cause rupture of the wall, and the urine be extravasated into the surrounding tissue, the peritoneal cavity, or into some of the neighboring organs, inflammation and previous adhesions having been formed.

The walls of the pelvis may be very much distended by the retained urine and accumulated pus, and the kidneys may undergo atrophy, as in hydronephrosis. Occasionally the fluid becomes entirely absorbed, the pelvis may shrivel into a hard capsule for its own inspissated contents, and the ureter become converted into a fibrous cord, its lumen having been obliterated. In certain cases where the inflammation has been very severe, a fibro-plastic exudation is thrown out upon the surface of the mucous membrane, and this has been termed a diphtheritic pyelitis.

Symptoms.—It must always be remembered that the symptoms of pyelitis are often masked by those of its cause. It usually begins with a chill, sometimes a series of rigors, followed by a rise of temperature of about three degrees Fahrenheit; pain in the back, increased on pressure and often radiating down along the course of the ureter. There is often nausea and vomiting, together with a continual desire to micturate, and pain on attempting to do so. As the disease progresses and becomes more chronic, the lassitude from which these patients suffer increases.

Hectic is finally developed and death ensues, either from exhaustion or a form of septicæmia, or by the combined action of both.

In those cases due to a renal calculus, the pain in the loins is the most prominent symptom.

Another quite diagnostic symptom is the alternating discharge of the clear or normal urine, and that charged with pus.

Urinary Examination.—The urine is usually increased in quantity, owing, perhaps, to the moderate hyperæmia of the kidneys always associated with this disease. The specific gravity is somewhat above normal, from 1.025 to 1.030; and its reaction is alkaline. Under the microscope, it is found to contain blood, pus, and epithelial cells.

Great stress has been laid upon the character of the epithelial corpuscles in the urine and their diagnostic significance in reference to pyelitis. But from the observations of Dr. Credon and others, it has

been clearly proven that there is no difference in the size and shape of the epithelial cells in the different regions of the genito-urinary tract. For this reason, it becomes absolutely impossible to base any positive diagnosis of pyelitis upon anything found in the urine with the microscope. Albumin will always be found on account of the pus present.

In some cases, the urine and the pus is retained in the pelvis of one kidney for a time, and the urine excreted by the other kidney will appear normal, or the two will alternate.

In other instances, the urine is permanently retained in the pelvis of one kidney; under such circumstances, there will often be formed a pyelo-nephritic tumor in the lumbar region, which will produce a bulging of the side between the crest of the ilium and the twelfth rib. There will be deep-seated fluctuation which can be detected upon palpation; with tenderness upon pressure, and flatness upon percussion, except when the tumor is crossed by the colon containing gas. If tapped, a sero-purulent fluid may be obtained, but with all the above symptoms the urine may remain normal or free from pus.

A mild form of pyelitis is far more frequent than the severe type just described. It is often mistaken for and treated as a cystitic inflammation.

This variety is often chronic, when it unquestionably acts as an exciting cause for the development of intrinsic renal lesions. Its characteristic symptoms are the passing of pale *acid* urine, which has a low specific gravity and contains albumin and pus-corpuscles. The urine from a case of chronic pyelitis contains a fair amount of pus, while the reaction remains strongly acid; with a cystitis, the urine contains pus in abundance, but the reaction is alkaline.

From the study of a large number of these cases, this conclusion has been formulated. When a patient has increased micturition and has to rise several times during the night to empty the bladder, and the urine passed is strongly acid, with a considerable quantity of pus and some albumin but no casts, the inflammation is located in the pelves of the kidneys.

These cases are frequently kept up by an undue acidity of the urine.

Diagnosis.—This is exceedingly difficult to make with certainty. If the patient has, along with the above symptoms, alternating intervals of purulent and clear or normal urine, the diagnosis of pyelitis is pretty certain to be confirmed at the necropsy. This phenomenon occurs in connection with those cases due to renal calculi or plugging of the ureter with mucus or inspissated pus. On the other hand, it should be remembered that this fluctuation is not always present.

The continuous discharge of acid urine containing pus is positively diagnostic of pyelitis.

Prognosis.—This depends in a great measure, if not wholly, upon the exciting cause. When it is a complication of chronic cystitis, enlarged prostate, urethral stricture, and operations upon the genito-urinary tract, the prognosis is very unfavorable, to say the least. When pyelo-nephrosis occurs, the tumor may disappear, the sac be obliterated, and the patient recover, but it ruins one kidney; if this does not take place and no rupture follows, death may be expected from exhaustion or septic toxæmia. Should the sac rupture, the prognosis will depend upon the seat of the extravasation; if it is into the peritoneal cavity or retroperitoneal areolar tissue, death will ensue from shock, peritonitis, or septicæmia; if externally or into the alimentary tract, the patient may and frequently does recover. If both kidneys are the seat of a pyelitis, the case is almost certain to terminate fatally, but when only one is implicated, there is always a chance for recovery.

Treatment.—During the onset of the disease, wet or dry cups to the loins, followed by warm poultices, should be employed and morphine should be injected hypodermatically if the pain be very severe and unbearable; considerable care, however, must be exercised in the use of opium in any form, for in some it certainly does excite a fatal uræmia. Alkaline and demulcent drinks should be administered freely, as they diminish the irritability of the urine.

The following mixture has been found one of the most valuable of all, not alone in inflammations of the renal pelvis, but in all forms of catarrh and inflammation involving any portion of the mucous membrane of the urinary tract. This statement is especially true in regard to the bladder. For it appears quite clear that a large proportion of the inflammatory conditions of this canal, not due to a calculus or some mechanical obstruction, are in a great measure dependent upon a depressed or over-worked condition of the lumbar portion of the spinal cord, and to a similar condition of the abdominal sympathetic system, and especially of the hypogastric, renal, and vesical plexuses, in connection with an acid condition of the urine.

If we overcome these three difficulties, restore the cord and sympathetic system to their normal state, and remove the irritability of the urine, the inflamed mucous membrane will by nature's intrinsic reparative powers be speedily restored to its normal condition.

This combination fulfils these three indications and is usually followed by immediate relief:

℞ Extracti Damianæ Fluidi...................... ℨ vi.

Extracti Hyoscyami Fluidi............... ...... ℨ iij.

Potassæ Bicarbonatis.......................... ℥ ss.

Acaciæ..q. s.

Aquæ destill..........................q. s. ad ℥ iij.

M.   Sig. ℨ i. four times a day in water.

By the addition of the mucilage, the insoluble extracts form with the alkali an emulsion. The damiana is one of the most powerful stimulants to a depressed or over-worked spinal cord; while in health it has but little, if any, influence. The so-called antispasmodic action of hyoscyamus is due to its power to stimulate a weakened sympathetic system, and in these cases it acts by this stimulating property, and raises the depressed and irritable hypogastric and renal plexuses to their normal standard and activity. The alkali renders the urine less irritating.

The hyoscyamus and potash are not new agents, but the damiana is, and it is a remedy greatly needed in many of these cases, for they are frequently excited by venereal excesses. Hot baths, especially hip baths, and perfect rest must be insisted upon. One of the best methods for a medicated sitz-bath is to put a bunch of wormwood in a chamber or other receptacle in a closed water-closet chair, and then pour on it some boiling hot water, and have the patient sit over the steaming decoction. This valuable suggestion was made by Prof. Satterthwaite.

If the disease becomes chronic, with the excretion of large quantities of pus, astringents, especially gallic acid, will be found useful, and in all a nutritious non-stimulating diet must be enforced.

In case pyonephrosis makes its appearance, aspiration is the only mode of treatment at first, both to prove the correctness of the diagnosis and to lessen the immediate danger from rupture into some locality where a fatal result would be almost certain to ensue; later, if the tumor reappears, it may be expedient to make a free and permanent opening through the abdominal wall.

Counter-irritation to the lumbar region in the form of actual cauterization is often followed by a great improvement.

As an undue acidity of the urine often exists and keeps up the inflammatory action, the digestive apparatus requires attention, that the quantity of uric acid produced may be diminished.

The inspissated bile pill will be found a most effectual remedy, see

PYONEPHROSIS.

Definition.—Pyonephrosis is that condition in which a pyelitis has become chronic, the ureter occluded, the renal pelvis distended with pus, and the kidney-tissue liquefied and destroyed.

Etiology.—The indirect causes are those which excite a pyelitis, but the direct cause is the occluding of the ureter. In fact, it is one of the ways in which a pyelitis may terminate.

Pathological Anatomy.—The mucous membrane of the pelvis of the kidney is thickened, the ureter occluded, and the pelvis, infundibula, and *calices* over-distended with pus. The renal substance is gradually encroached upon, the papillæ flattened and destroyed, and finally the Malpighian pyramids and the cortical arches are completely obliterated.

The capsule of the kidney becomes distended and thickened, and forms the wall of a sac containing pus and granular débris.

Symptoms.—It is preceded by all the symptoms of an ordinary pyelitis, followed by a disappearance of the pus in the urine, and the progressive development of a tumor in the lumbar region.

The tumefaction is upon one side or the other, and occupies the space between the crest of the ilium and the floating ribs. As a result, the abdomen becomes unsymmetrical. On palpation, a deep-seated fluctuation and considerable pain are found to be present. Upon percussion, an increased area of dulness is easily detected, which is often crossed by a resonant zone, indicating the position of the colon. Aspiration will give evidence of pus or purulent débris.

Diagnosis.—This rests upon the previous history, and the removal of purulent matter by a trocar or aspirator.

Prognosis.—Recovery is possible if the sac bursts into the alimentary tract, or externally through the abdominal parietes.

In case it bursts into the retroperitoneal tissue or peritoneal cavity, death speedily ensues.

In other instances, there is no rupture, the suppurating foci continue, and the patient dies from exhaustion. In still others, the formation of pus ceases, absorption takes place, the sac contracts down upon a cheesy mass, and recovery results.

Treatment consists in good food and tonics, aspiration, nephrectomy or nephrotomy.

HYDRONEPHROSIS.

Definition.—Hydronephrosis is that condition in which the pelves, infundibuli, and calices of the kidneys are distended with urine, owing to some obstruction in the urinary passages, almost invariably of the ureter, followed by complete or partial atrophy of the renal substance. Both pelves are seldom affected at the same time.

Etiology.—Congenital malformations play an important part in the causation of this condition, and are often associated with deformities elsewhere, such as hare-lip, imperforate anus, etc. The causes, however, which occur after birth, and which may be called acquired, are the impaction of calculi, inflammation in the walls of the ureter obliterating its lumen by contraction, pressure by tumors, morbid growths or displaced organs, as the uterus or enlarged ovary, pelvic peritonitis with exudation of fibro-plastic material, inflammation of the bladder involving one or both orifices of the ureters, and obstructions of the urethral canal. Hydronephrosis is usually unilateral, but where the cause exists below the cystic orifice of the ureters, it becomes bilateral and of a more serious nature. Even then it is more marked upon one side than the other.

Pathological Anatomy.—Obstruction of the ureter is followed by dilatation of its lumen, and an increase in the thickness and fibrous density of its wall. The renal pelvis progressively enlarges, and at the same time there is a progressive atrophy of the renal substance, due to the continued and increasing pressure of the continually effused fluid. The kidney-tissue never disappears entirely, but it can be found either in a thin stratum or in isolated patches upon the wall of the cyst, which, like the wall of the ureter, is converted into a thick and fibrous layer.

The cyst in some cases becomes quite large, measuring several inches in diameter; it is usually single, but in some rare instances it is multilocular. These multilocular formations are due to an irregular dilatation of the uriniferous tubules. Their fluid contents are light

in color, and somewhat cloudy, low in specific gravity, alkaline or neutral in reaction, rarely acid, and almost always contain albumin and all the salts usually found in the urine, excepting, perhaps, urea and uric acid, which are sometimes absent. In rare instances, the contents of these cyst are gelatinous. Hydronephrosis of one kidney almost always produces hypertrophy of the opposite organ.

Symptoms.—During the early stage of development of a unilateral hydronephrosis, no symptoms are developed by which this condition can be diagnosticated. The unaffected kidney accomplishes the work formerly performed by the two, and consequently no change in the quantity or quality of the urine can be discovered, and suspicion is seldom excited, sometimes not until a tumor is found in the lumbar region, and even then there is often great difficulty in making the diagnosis. Should the tumor suddenly disappear, and its disappearance be accompanied by the discharge of a large quantity of turbid urine, the diagnosis is no longer in doubt.

There is usually a gradual loss of flesh and strength. Pressure by the tumor when large may cause embarrassed respiration, especially during recumbency and after eating, together with distention of the subcutaneous veins.

These or similar symptoms can occur with any abdominal tumor, but an examination of the fluid drawn from the cyst by an exploring needle removes all doubt as to diagnosis.

Rupture of the cyst is followed by collapse and death, while double hydronephrosis is soon followed by a fatal result with symptoms of uræmic poisoning.

Diagnosis.—This condition has to be differentiated from ascites, from hydatids, ovarian cysts, pyelo-nephritis, and pyonephrosis.

From ascites it is sometimes quite difficult to distinguish, especially if both kidneys are involved; an examination of the fluid is the only means for settling the question. That from the hydronephrotic cyst will contain the urinary salts, while that from ascites will not. It is often impossible to distinguish it from an hydatid cyst of the kidney unless the hooklets of the ecchinoccocus are found. If double, however, it is not likely to be due to a hydatid cyst. From the ovarian tumor it is diagnosticated by the history, its location, vaginal examination, and the character of the contained fluid.

It is distinguished from pyelo-nephrosis and pyonephrosis, by the presence or absence of pus in the contained fluid.

Prognosis.—So long as hydronephrosis is unilateral and the other kidney remains healthy, the prognosis is favorable so far as duration of life is concerned, but should any disease attack the other kidney,

the prognosis will be most serious. Rupture of the cyst-wall seldom occurs, and little inconvenience is experienced by the patient from the presence of the tumor. Bilateral hydronephrosis is of necessity fatal, unless the obstruction to the free escape of urine is quickly removed.

Treatment.—Absorption of the fluid cannot be produced by any medicinal means known at the present day. Manipulation of the tumor and abdomen along the course of the ureter may remove the obstruction, but great care should be exercised not to use sufficient force to rupture the sac of the cyst. Tapping with a small trocar and canula, or aspiration may be employed with good results, though the return of the tumor is almost certain. Nephrectomy or nephrotomy might be performed, should the symptoms be sufficiently urgent.

RENAL CALCULI.

Definition.—A renal calculus is a concretion formed in the tubules of the kidneys or in the renal pelves, by a deposition of one or more of the solid constituents of the urine. Calculi may occur at any time during intra- or extra-uterine life.

Etiology.—The precise cause of renal calculus is unknown, and although many theories have been advanced to account for its development, none are entirely satisfactory.

It is known, however, that every calculus has a nucleus of some foreign substance, such as pus, inspissated mucus, blood, pigment granules, or crystals of some sort, often uric acid. Renal calculi are usually composed of uric acid, but other kinds often occur, such as those composed of oxalate of lime, phosphates of lime, carbonate of lime, cystin, xanthin, and still others composed of several of these ingredients.

Pathological Anatomy.—In cases where there has been a deposition of crystals without the formation of large calculi, the kidneys upon post-mortem section have a streaked appearance, usually of brick-red color, owing to the presence of the uric acid in the tubules. If the concretion be large and yet retained in the substance of the kidney, it becomes the source of much irritation; congestion and inflammation are excited and often followed by suppuration and abscess; in fact, it acts as a foreign body would elsewhere. If, on the other hand, it passes from the kidney and remains in the pelvis of the organ, it becomes a fruitful source of pyelitis. By blocking up the opening to the ureter, it may produce hydronephrosis. In case the calculus becomes large, it may of itself press upon the renal substance, and in

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this way cause marked atrophy of the kidney. Passing from the renal pelvis down to the bladder through the ureter, it may there become the nucleus for the formation of a vesical calculus.

Symptoms.—Renal calculi which are retained in the pelvis of the kidney may increase to a very large size and even completely destroy the renal substance without having given rise to any sign of its presence during the life of the patient.

But usually there is pain in the lumbar region, which shoots down the groin and is aggravated by exercise or any jolting of the body. In the urine, blood, pus, epithelial cells, and often crystals, usually uric acid or oxalate of lime, are discovered. Sometimes a calculus may pass from the pelvis through the ureter to the bladder, and so out through the urethra without the patient's knowledge, but as a rule the symptoms are painfully severe.

When attacked by a renal calculus, the patient complains of intense shooting pains in the loins, radiating over the hypogastrium and down the inner side of the thighs. The testicle and the scrotum of the affected side are often retracted, and there is sharp pain there, as well as in the head of the penis. In the female, the labia are affected in like manner, but the female sex seldom suffer from renal calculi.

There is often nausea and vomiting, the patient is covered with a cold perspiration, the respirations are rapid and shallow, the pulse small, hard, and rapid, with great anxiety of countenance.

An attack may last for a few minutes only, or there may be remissions followed by recurrences, each one appearing to the patient to be more severe and serious than the one which preceded; but if the calculus remains lodged in the ureter, the symptoms gradually subside and hydronephrosis is developed.

Prognosis.—From the presence of a renal calculus in the pelvis of the kidney, no danger is to be feared so long as complications are not developed. Where they occur the prognosis rests upon the complication and not upon the presence of the calculus. A fatal result from renal calculi rarely occurs, unless by the induced suppression of urine, secondary to nervous exhaustion.

Treatment.—Many different ways have been proposed with the view to dissolving the calculus in situ, but none of them have been found reliable. Perhaps a hygienic mode of life is as sure a safeguard as anything in the way of a prophylactic. In the renal colic, baths as hot as the patient can bear, or hot applications over the abdomen and loins, relax the tissues and lessen the pain, but they do not arrest the muscular contraction on the part of the ureters as much as the administration of ether and chloroform. In conjunction with the

heat, the internal administration of full doses of belladonna and strychnia will diminish the irregular and spasmodic contraction of the muscular coat of the ureter, while the normal and even peristaltic action will be increased. By this method of treatment the rapidity of transit is increased.

Opium and anæsthetics are to be avoided, if possible. The anæsthetics tend to diminish the peristaltic action of non-striated muscle fibres, and hence prevent the movements of the calculus along the ureter. They will, of course, relieve the pain, but when the patient recovers from their influence, they are no better, and the stone has made little or no progress in its descent. They are of service in relaxing the tissues and giving the patient a rest.

The opium is equally inefficient, for the same reason as the anæsthetics, and besides it has a dangerous element. To completely alleviate the suffering, enormous doses of the drug may be required. If now for any reason the calculus should slip through into the bladder, the necessity for the opium at once disappears, and the patient may become suddenly narcotized, which might prove both a troublesome and serious, if not a fatal complication. For this reason, great care should be exercised in reference to the quantity of opium administered either by the mouth or hypodermatically.

In cases where a calculus is retained in the pelvis, and complications make their appearance, nephrotomy is the only treatment that will afford relief.

The recurring attacks of renal colic may be caused to disappear by giving the patient one minim of glacial carbolic acid three times a day. But a more satisfactory plan of treatment is to place the individual upon a limited nitrogenous diet, as for instance, one composed of skim-milk or butter-milk. At the same time giving the bile pill and the damiana mixture (see pages 26 and 125).

ACUTE AND CHRONIC ATROPHY OF THE KIDNEYS. HYPER-
TROPHY OF THE KIDNEYS. CYSTS OF THE KIDNEYS.

ACUTE ATROPHY OF THE KIDNEYS.

Definition.—This is a disease that has been described as one in
which the kidneys rapidly diminish in size, owing to a rapid exuda-
tion into the cells of the organs, followed by fatty degeneration and
disintegration. The cause is unknown: it is characterized by a copi-
ous albuminuria and casts, and frequently with marked uræmic symp-
toms, terminating in death.

Etiology.—The causes of this disease are unknown, but they appear
to be dependent upon blood poisoning, and acute hepatic diseases.
It has been described as associated with acute yellow atrophy of the
liver, when it usually follows, but may precede the hepatic lesion. It
is said to be more frequent in the female than in the male. It has
been met with during pregnancy and after confinement.

Pathological Anatomy.—In many respects this lesion closely resem-
bles acute atrophy of the liver.

The disease has been described as having two stages. In the *first,*
or that of exudation, infiltration, and enlargement, the organs are
not markedly congested, their capsules are not adherent, and the un-
derlying renal surface remains smooth, but soft and flabby. The cor-
tical substance is swollen, and the tubules enlarged and white.

Upon *microscopic examination,* the vessels are usually found empty,
and compressed by the swollen epithelium of the tubules.

The tubes are occupied by a dense opaque material, the individual
cells are swollen and granular, their nuclei being hidden by the mo-
lecular cell contents. Both medullary and cortical portions are
involved. Some of the cells are in a state of fatty degeneration, or
even broken down.

In the *second* stage, the organs are still paler and their capsules
wrinkled.

Where *examined microscopically,* the stroma is found to be intact,

the blood-vessels empty, and the tubules in various stages of retrograde metamorphosis; some being more advanced than others. These changes are identical with those found in the hepatic cells in acute yellow atrophy.

Symptoms.—Little seems to be known of the symptoms, but they are, so far as studied, a diminution in the quantity of water, abundant albuminuria, and a large number of casts.

There is also a tendency to jaundice, hemorrhagic extravasations, and uræmia—in fact, all the symptoms are those of the latter condition.

Diagnosis.—Rather than place this condition under a special classification, it should be considered as a very severe type of the acute parenchymatous metamorphosis of the kidneys, as its etiology, pathological anatomy, and symptoms are precisely like those of a severe acute parenchymatous metamorphosis.

Prognosis.—This is unfavorable.

Treatment.—The preventive measures applicable to acute parenchymatous metamorphosis of the kidneys are doubly applicable here. But no therapeutic agent or other means have been found by which this rapidly progressing cellular transformation can be arrested or modified and the renal organs enabled to regain their former functional activity.

CHRONIC ATROPHY OF THE KIDNEYS.

Definition.—Here, as in the acute form, the term applies to the diminution in size which is usually associated with several forms of renal lesions. The term is more a synonym than a specific lesion. That form associated with hydronephrosis approaches closely to a true atrophy of the renal substance, but all the other forms are a stage of some other disease.

Etiology.—The causes are hydronephrosis, the pressure of a tumor external to or within the gland, enlarging calculi within the renal pelvis, or pressure upon the vessels entering the kidneys.

Pathological Anatomy.—Following the dilatation of the renal pelvis, the kidney is replaced by a large, lobulated mass or series of cysts, containing a watery fluid. At first the Malpighian pyramids are flattened, but later the cortical layer also disappears. This form of atrophy occurs on one side, associated with a compensatory hypertrophy of the opposite kidney. There are no special symptoms and the lesion is only a part of other diseases.

HYPERTROPHY OF THE KIDNEYS.

Definition.—Hypertrophy of the kidneys is that condition in which all the elements of the organs are increased in size, and possibly in number or both.

Etiology.—This condition is usually caused by long-continued congestion, from which every element of inflammation has always been absent, and hence occurs from congenital absence of one kidney. It is also the result of hydronephrosis or pyelo-nephrosis on one side, or a tumor, or any disease by which one kidney is diminished or destroyed and the other left intact, to do the work previously accomplished by the two. The term hypertrophy is loosely applied to almost every enlargement of one or both organs from any cause, but this is not a correct usage. True hypertrophy is limited to a physiological increase in size, with the production of normal, and not congestive and inflammatory material. Its weight may reach eight or ten ounces (226.796 or 283.496 grams) or more. The renal artery and vein will be found proportionately enlarged.

Symptoms.—There are no symptoms connected with this condition.

Physical examination may in some few cases enable the physician to make out the existence of an enlarged kidney, but the diagnosis is uncertain and in most instances unsatisfactory. Should such a condition be discovered or even suspected, the prognosis is always favorable and no treatment is called for. This change is, strictly speaking, a post-mortem revelation.

RENAL CYSTS.

Definition.—Cysts of the kidneys are so called when one or more thin fibrillated connective-tissue sacs, containing a clear, faintly yellow serous fluid, are found in or protruding from the substance of the glands.

Etiology.—The precise cause for these formations is not known, excepting when they are congenital.

Pathological Anatomy.—There are four distinct varieties :

The *first* or congenital, are developed in the kidneys of the child in utero. This is caused by the obliteration of some part of the urinary tract, and is said to be due to the formation of connective tissue between the calices and the papillæ.

Both organs are usually involved and converted into cystic masses, which in some cases become very large, rendering evacuation necessary before the child can be delivered.

This form of cystic transformation seems to have originated princi-

pally in the Malpighian tufts, the capsules of which are enormously distended and the vascular supply atrophied.

In the *second* variety, we find one or more cysts in otherwise perfectly normal kidneys. The cysts may be small, or of considerable size. In either case the wall of the sac is composed of a very thin layer of dense fibrillated connective tissue, lined by a thin layer of flat cells.

Their fluid contents are composed of a perfectly clear, light, straw-colored serum which does not contain albumin nor any of the urinary solids.

The *third* variety occurs with the various chronic renal lesions, especially with the sclerotic and atrophic form of the chronic diffuse nephritis. The formations are, more strictly speaking, retention cysts, being formed either by the plugging of a uriniferous tubule or by a strangulation produced by the contraction of the newly formed connective tissue. The wall of these cysts not infrequently retains an internal coating of the original cells of the uriniferous tubule from which they have been developed.

The *fourth* variety is a cystic degeneration of the kidneys proper. Both glands, as a rule, are implicated. Both become enlarged, and are now composed of cysts of all sizes and colors.

These sacs contain serum, fibrin, colloid material, and may and do go on to suppuration, when they also contain pus.

Hemorrhage into these cysts also occurs.

The surface of the kidneys will be nodular, and very little true or normal renal substance will be found. The little which is left may be perfectly normal, compressed, atrophied, or in a suppurating condition.

This lesion is supposed to be due to a new growth originating between the lobules, and is usually a post-mortem discovery.

Symptoms.—In all four varieties the symptoms are obscure, and the formation of a large tumor in the region of one or the other kidney is the only prominent one, and even this is not diagnostic.

Diagnosis.—This is most frequently made at the necropsy.

Prognosis.—In the second form it is good. In the first and fourth forms it is always fatal. The third depends wholly upon the disease with which it is associated.

Treatment.—The first, second, and fourth forms require none. In the third, it is that of the chronic renal disease.

CHAPTER XII.

TUBERCULOSIS OF THE KIDNEYS.

SCROFULOUS KIDNEYS. RENAL PHTHISIS.

Definition.—Renal tuberculosis is that condition in which the kidneys, renal pelves, and the ureters are the seat of a tubercular inflammatory infiltration. It may develop in the form of miliary tubercles along the course of the vessels of the cortical substance and pyramids of Ferrein, but more frequently it occurs in the form of large caseous masses, which may be located in any portion of the kidneys, the renal pelves, or ureters.

Etiology.—The precise origin here, as in other portions of the body, is not known, except by those who accept the Bacillus tuberculosis as the causative agent. Renal tuberculosis is developed in connection with an inherited or acquired scrofulosis or tubercular diathesis, and may be either primary or secondary to a similar condition in the lungs or other parts of the body. It is more frequent in childhood and youth than in advancing years. But when found late in life, it is usually in the form of cheesy masses of secondary origin. It is more frequent in males than females, and does not always attack both organs, but when both are involved, the disease is always more advanced in one than in the other. The right kidney is the gland most frequently implicated, and when the two are invaded, the greatest damage is usually done to the right. Occasionally one kidney may be completely destroyed by the tubercular process, while the opposite gland remains absolutely free from disease.

Pathological Anatomy.—The microscopic appearances will differ in the two forms. If miliary tubercles only be present, the organs will not be much enlarged. The external and the cut surfaces will be dotted with small white glistening bodies, which are scattered throughout the cortical substance, but are rarely found in the pyramids of Malpighi. As the disease advances, these miliary tubercles coalesce, their centres undergo retrograde metamorphosis and caseation, and in this way form

large cheesy nodules. These larger masses are in all probability developed in some cases without the intervention of the miliary form.

In another variety, this peculiar inflammation commences in the calices of the pelvis, which, with the apices of the pyramids, are converted into a caseous mass of yellowish color, identical with tubercular or scrofulous masses in other parts of the body. The process progressively extends to the Malpighian pyramids and the surrounding cortical substance. In this way the kidneys become enlarged, the renal tissue destroyed and replaced by tubercular new-formations, either tubercular tissue or cheesy masses.

In some extreme cases where both the renal pelves and kidneys are involved, the neoplasm, having but little vitality, readily dies, undergoes liquefaction, and forms cavities containing thin pus and cheesy débris. It is by this process that the kidneys are converted into a bag of pus, sometimes as large as a child's head.

Microscopical Examination.—The small miliary bodies, when studied in thin sections, are found to be composed of zones of altered renal tissue. At these points the intertubular tissue is infiltrated with small round corpuscles. The epithelial cells of the involved tubules degenerate, and the basement walls of the tubes collapse, or are obliterated by the abundant cell-formation. In some sections, the reticulated or adenoid tubercular tissue, round, oval, and giant cells will be found. But more frequently the central portion of the small granulation has undergone a caseous transformation, while the periphery is still composed of this aggregation of small round and oval corpuscles. The larger tubercular masses are either formed by the coalescence of smaller masses or are of independent development. The microscopic appearances are the same in either case.

The principal differences between the miliary and cheesy masses is the preponderance of the caseous disintegration in the latter.

Symptoms.—These are usually quite obscure. When the tubercles occur in small quantities in the kidneys, or when the tubercular inflammation is not extensive, all tangible symptoms of the disease are absent. But as the process develops and involves larger areas, a rise of temperature will be developed with some pain and tenderness over the region of the kidneys. On percussion, increased dulness may be discovered, and if the walls of the abdomen are thin, a tumor may be made out by palpation. Hectic fever and progressive emaciation rapidly ensue, together with chills, night-sweats, and the other usual accompaniments of pulmonary tuberculosis. Frequently we have all the rational signs of pulmonary phthisis, the cough excepted,

but with an absolute absence of all the physical signs; in such in-
stances renal tuberculosis should be suspected.

In some cases, the testicle is first attacked, and followed by the
renal lesion.

If there is an associated cystic tuberculosis, micturition is often
frequent and painful.

The urine is not often altered early in the disease, but later it may
become alkaline and filled with débris of the renal substance. The
bacillus tuberculosis is said to be diagnostic of the disease if found in
the urine.
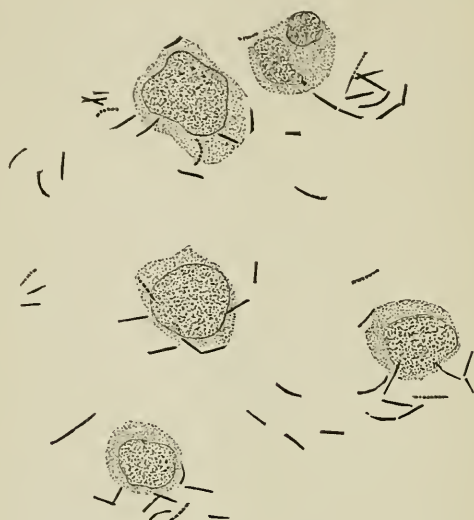
Fig. 28.—Bacillus Tuberculosis.   × About 850.

Delafield and Prudden, "Handbook of Pathological Anatomy and Histology."

Method for Staining the Bacillus Tuberculosis.—The method for
staining the Bacillus tuberculosis is as follows:

First, make a saturated solution of aniline oil in water, 1 to 15,
shake for five or ten minutes and then filter.

Second, make a saturated alcoholic solution of Gentian violet.

The urinary débris is drawn up with a pipette and a drop deposited
upon a clean cover glass and allowed to dry on the surface, or two
covers are rubbed together, thus producing an even film.

From 5 to 10 ℔ (0.32 to 0.64 cc.), of solution No. 2 is added to
one ounce (31.1 cc.) of solution No. 1 until the top assumes a metal-
lic lustre.

The prepared cover or covers are floated in this mixed fluid for

twelve hours, the side containing the specimen facing the staining fluid.

The cover containing the specimen is next immersed in a 25% aqueous solution of nitric acid for half a minute.

It is then soaked in a 60% solution of alcohol for half an hour.

It is then dried either with or without the use of an alcoholic or gas flame.

When dry, it is stained in a solution of vesuvin or Bismarck brown for two minutes, then washed in ordinary alcohol, dried, and mounted in Canada balsam or dammar varnish.

Sections made from the kidney may be stained in the same solutions.

In either case, if the bacilli are present, they will appear under the microscope as blue rod-like bodies, varying in length from one-fourth to one-half the diameter of a red blood-cell. They may have a beaded appearance or may be slightly curved.

A number of other methods have been recommended, but this one will usually secure the desired result.

Upon microscopic examination, the urine will be found to contain epithelial cells, pus, blood, granular matter, and shreds of broken-down tubercular tissue. If the latter are distinctly made out, the diagnosis is fairly certain. Albumin and casts and many of the evidences of ordinary renal lesions may also be present.

The relative merits of the bacillus tuberulosis as a diagnostic aid has not as yet been fully established. In the majority of cases of genito-urinary tuberculosis in which they have been sought for, they were found to be absent.

The urine is occasionally suppressed and the symptoms of uræmic poisoning are developed and followed by a fatal result.

Diagnosis.—It is exceedingly difficult to diagnosticate this lesion with any degree of certainty. But when a patient presents all the rational signs of phthisis and the physical examination of the chest is negative, without any evidence of cerebral, laryngeal, or peritoneal tuberculosis, it is well to suspect a renal form and to examine carefully the lumbar region and the urine for some evidence of disease in the kidneys or genito-urinary tract. Even this is very unsatisfactory, as the urine contains no positive evidence, except tubercular tissue, which in itself is difficult to recognize.

If the bacilli were positively diagnostic and readily found, the diagnosis would be easy and certain.

If, however, the urine contains pus, blood, and fragments of cheesy material, and one chances to find the bacilli with the above clinical history, the diagnosis is tolerably correct.

The disease usually runs a very slow course, and the patient may die of some intercurrent disease.

Scrofulous or tubercular nephritis is frequently a microscopic revelation. One of the most perfect examples observed occurred in an accident case. In that instance, it was found at the necropsy that both kidneys, ureters, bladder, and prostate gland were a mass of tubercular tissue. The patient, however, had died as the result of a broken neck.

Treatment.—When discovered during life, the same treatment that is proper for general tuberculosis is to be instituted: pure air, nutritious food, and tonics, and particularly the syrup of the iodide of iron. Cod-liver oil is usually detrimental in this as in all tubercular processes, from the fact that in the majority of instances it upsets the digestive apparatus, and prevents the assimilation of other substances. Fats also are non-nutritious substances—that is to say, they do not reproduce in the system albuminoid substances or tissues, their function being that of heat-producing agents, lubricators, and energy-yielding elements.

Change in climate may be found the most useful of all agents. The change should not be for a few weeks or months, but for a lifetime, if it is expected to give the best result. The patient should travel from place to place until that climate is reached which suits the individual constitution, and there remain.

As soon as the testicle gives evidence of tubercular inflammation, it will not be of any use if allowed to remain, and for this reason and the possibility that it precedes and sometimes excites the renal tuberculosis, it should be extirpated.

INFARCTION OF THE KIDNEYS. FAT EMBOLISMS OF THE KID-
NEYS. PYÆMIC EMBOLI OF THE KIDNEYS.

INFARCTION OF THE KIDNEYS.

RENAL EMBOLISM.

Definition.—Renal embolism or infarction is that condition in which a terminal artery of the kidney substance has become occluded by a non-irritating embolus.

Etiology.—The chief cause of this lesion is valvular disease of the heart. The emboli may come from the cardiac valves in the form of detached fibrin or atheromatous material. They may also originate from arterial thrombi, aneurisms, or atheromatous patches. This condition has been called "rheumatismal nephritis." Infarctions may be single or multiple.

Pathological Anatomy.—As the result of the lodgment of the embolus, we have the circulation cut off from a conical or wedge-shaped area, which first becomes anæmic.

The anæmia lasts only a short time, when the blood returns into this pyramidal space from the venous side, and a permanent congestion is established.

The embolus, with the surrounding stasis, acts as a foreign body, and may terminate in a number of ways.

When small and non-infective, they rarely cause suppuration.

If small, the coagulated blood of the infarction becomes gradually decolorized, changing from dark red to brown and finally to a yellow int; it is ultimately absorbed. A moderate degree of inflammation ensues, which results in the formation of new tissue; and finally all that remains to mark the seat of the infarction is a cicatricial pit or depression.

In other cases, especially when the territory involved is large, there is, following the decoloration, a molecular disintegration and partial softening which excites an active peripheral inflammation. This

zone is rapidly encapsulated by a band of newly formed connective tissue, thus preventing a complete fatty degeneration and absorption; but the watery constituents of this granular mass are absorbed, and a gray semi-solid or solid substance remains.   Its surrounding capsule becomes firmer and continually contracts upon this conical mass until a dry granular and prominent wedge is formed.   The apex is imbedded in the cortical substance of the kidneys, but the base often protrudes beyond the free surface of the glands.   Immediately around the infarction there is usually found a zone of hyperæmic tissue.

In still other instances, this dry and granular infarction may be

FIG. 23.—ACUTE CONGESTION OF THE KIDNEY, WITH MULTIPLE INFARCTIONS.
A. Medullary portion. B, Cortical portion. a, Infarctions. b, Congested Malpighian corpuscle.

found to contain an abundance of inorganic salts, when it is spoken of as a chalky or calcareous nodule.   This change, however, is exceedingly rare.

Symptoms.—As a rule, the lodgment of an embolus in the renal tissue does not produce symptoms active enough to attract attention. But occasionally during the course of a severe lesion of the cardiac valves, or with extensive atheroma of the large vessels, the individual will be attacked suddenly with albuminuria, renal hemorrhage, or both, associated with a marked rise in temperature and great pain in the back.

With such a history, the symptoms would justify the diagnosis of infarction of the kidneys, and in all such cases its probability will be confirmed by a necropsy.

Diagnosis.—As a rule, none is made at the time of occurrence, nor during the life of the patient. Infarctions of the kidneys are usually necropsy discoveries.

Prognosis.—The prognosis is favorable.

Treatment.—None need be instituted.

FAT EMBOLISM OF THE KIDNEYS.

Definition.—Fat embolism of the kidneys is a condition in which one of the terminal arterioles becomes occluded with an embolus composed of fat globules.

Etiology.—Occlusion of the small vessels by fat (fat embolism) appears to have been first observed by H. Müller, in 1860.[1] He found some of the choroidal vessels filled with fat, but did not at that time attach much importance to the condition.

The discovery, however, of fat embolism is credited to Zinker, in 1862. Since that time, numerous cases have been reported as occurring in the lungs, kidneys, and other organs of the body. They are more frequently found in the lungs than in the kidneys.

When they do occur in the renal tissue, they are frequently secondary to those deposited in the lungs, and are found two or three days later.

Fat emboli occur in connection with simple and compound fractures, especially the latter, and in those in which the cranial bones are implicated, also in connection with pyæmia and after surgical operations. In some cases of diabetic coma, similar formations have been described. In all cases, fat embolism appears to be associated with some form of blood taint which allows the fat to circulate in the blood in an undigested or free state, and consequently it is arrested and occludes some of the small arterial or capillary vessels in the various organs.

Pathological Anatomy.—The microscopic appearances are variable; the principal change is pallor of the whole organ, or marked zones of paleness. There is also some increase in the size, with a flabby condition of the organ. In some instances, minute hemorrhages will be found under the capsule.

Microscopic examination shows that certain portions of the kidneys are congested, while the remainder is normal. Near the congested

[1] Würzburger Medic. Zeitschrift.

areas, zones of fatty masses are found which, if the section has been stained with osmic acid, appear under the microscope as little black masses, some of which are located in the small capillary vessels of the glomeruli, or they may be in the small vessels just outside the tuft.

In the immediate vicinity of the congestion, small extravasations of blood will be noticed in which numerous fat droplets are found.

As a rule, fat is not present in the lumen of the uriniferous tubules, but the epithelial cells lining the tubules often contain fat droplets of large size.

Symptoms.—From the experimental researches of Scriba, the symptoms produced by fat emboli are as follows: The presence of fat in the urine at intervals; transient attacks of dyspnœa; lowering of tempera-
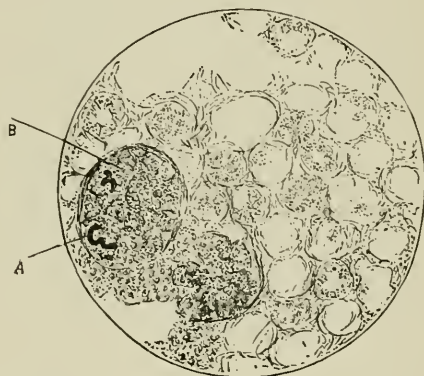
FIG. 30.—FAT EMBOLISM OF THE KIDNEY. × 350. SECTION STAINED WITH OSMIC ACID.

A, Capillary vessel in Malpighian tuft occluded by fat embolism, which is stained black by the acid; B, portion of tuft not occluded by the fat embolism.

ture; temporary and slight hæmoptysis, without fever, and generally without dulness or *râles;* irregular action of the heart; collapse, with marked pallor of the skin and mucous membranes; at first shallow respiration, at times interrupted by deep sighing inspiration, later *Cheyne-Stokes* respiration; spasm of various kinds or paralysis, generally bilateral; and diminution of reflex irritability.

Diagnosis.—A case presenting the above symptoms, in conjunction with one of the known causes, would be strong evidence in favor of fat embolism.

Prognosis.—This is usually, if not always, unfavorable. Scriba believes from his experience that death occurs when the fat emboli reach or attack the cerebro-spinal centres.

Treatment.—Little can be done, except to treat the pre-existing disease.

PYÆMIC EMBOLI.

Definition.—This is a condition of the kidneys in which an embolus charged with pyæmic poison has become impacted in a terminal artery, resulting either in the formation of a secondary metastatic abscess or a localized gangrenous patch of renal tissue. This condition, as a rule, does not give rise to any special symptoms during the life of the patient.

Etiology.—This form of abscess is always developed by the lodgment of some of the infectious or pyæmic poison at a given point.

Pathological Anatomy.—The kidneys may be the seat of one large suppurating mass, but usually they are dotted by numerous white points or small abscesses.

If the kidneys are removed early in the disease, the intermediate stage may be obtained, viz., wedge-shaped zones of red consolidation, or a little later the dusky gray masses of inflammatory exudation. In this form of infarction, the occluding embolus is not found at the apex and near the periphery of the organ, but is now central and completely surrounded by the diseased process.

In rare cases, instead of a suppurating focus being developed, the renal tissue becomes gangrenous in patches, with more or less surrounding suppuration.

Symptoms and Diagnosis.—Pyæmic suppuration of the kidneys is suspected if, during the course of a pyæmia, the urine suddenly becomes albuminous or bloody.

Prognosis and Treatment.—It is always a fatal disease and little can be done in the way of treating the general symptoms; they are usually, if not always, fatal.

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CHAPTER XIV.

TUMORS OF THE KIDNEYS: SARCOMA; CARCINOMA; ADENOMA; FIBROMA; CONGENITAL RHABDO-SARCOMA; ANGIOMA; LIPOMA; LYMPHOMA; OSTEOMA; ANGIOMA OR CAVERNOUS NEOPLASMS.

SARCOMA OF THE KIDNEYS.

Definition.—This is a condition in which the kidneys are the seat of a new growth of the embryonic connective-tissue type.

Etiology.—The absolute causation of sarcomata in the kidneys, as elsewhere, is unknown. This condition has been met with both in children and in adults, but it is more common in children. There appears to be considerable ground for believing that many of the cases published as primary carcinoma of the kidneys have in reality been sarcomata.

Only once has the opportunity presented for holding a necropsy in a typical case of primary sarcoma in an adult.

Pathological Anatomy.—The kidneys become very much enlarged, but they retain the general outline of the glands. The weight of the tumor may be as high as 50 or 60 ounces (1,417.488 or 1,700.972 grams).

In one case, previously recorded, the left kidney weighed 48 ounces (1,360.780 grams). When bisected, it measured in its long diameter, from the superior to the inferior border, 5 inches (13 centimetres); from the peripheral surface of the cortex to the pelvis at the apex of a pyramid, 3½ inches (almost 9 centimetres).

In this case the capsule was very much thickened; the pelvis was obliterated, the space being filled with a grumous material; the ureter was dilated and very much hypertrophied.

Upon *microscopic examination,* very little renal tissue was found, but the mass of the neoplasm was composed of medium-sized, round connective-tissue corpuscles imbedded in a homogeneous matrix.

In this particular case, the right kidney also contained a similar new growth; but on this side about one-half the renal tissue was plainly visible, and in a fairly normal condition.

The retroperitoneal glands were not implicated. A portion of the stomach, duodenum, and colon, lying against the large tumor, had become adherent to it, and were becoming invaded by the sarcomatous growth. The diaphragm was also involved in the morbid process.

There was no way in which the new development in one kidney could be traced to the opposite organ, except through the medium of the vascular channels. A similar primary sarcoma of the kidney was once found in a cow. This case was presented at the New York Pathological Society, 1880.

Symptoms.—The symptoms of sarcoma and carcinoma of the kidneys appear to be about the same ; namely, a rapidly growing tumor in the region of the kidneys, with recurring attacks of hæmaturia.
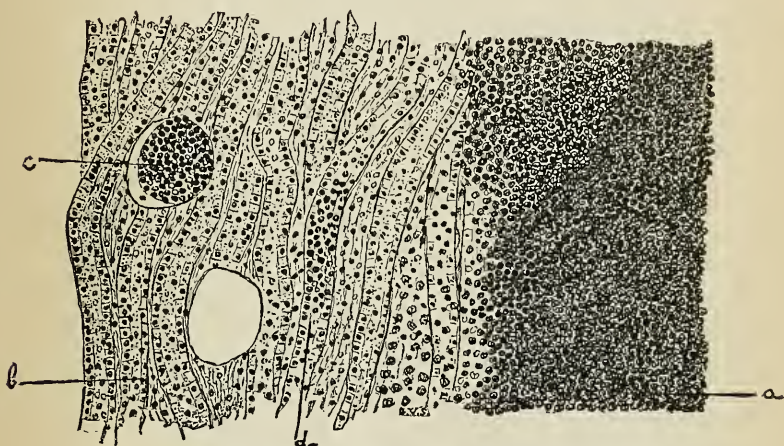
FIG. 31.—ROUND-CELL SARCOMA OF THE KIDNEY. × 350.

a, Sarcomatous tissue; *c*, Malpighian corpuscles in partially uninvaded tissue; *b*, uriniferous tubuli; *d*, renal tissue adjacent to the sarcomatous tumor, slightly infiltrated with sarcomatous cells.

So far as can be learned from the literature upon the subject, the sarcomata are attended with much less pain than the carcinomata. The sarcomata being the more vascular of the two, will in all probability give rise to more copious and frequent attacks of hæmaturia.

Few cases have been recorded. Dr. Abraham Jacobi, in presenting a sarcoma of the kidney in a child at the Obstetrical Society, 1874, remarked that he had not been able to find a recorded case either in in a child or an adult.

At one of the meetings of the New York Pathological Society in

1885, Dr. Jacobi, in presenting a similar case in behalf of a candidate, remarked that "there were only sixteen or eighteen cases of unquestioned primary sarcoma of the kidneys on record."

Secondary sarcoma, or those developing near the renal glands and growing into their substance, are not uncommon.

In sarcoma of whatever variety, there is not as characteristic a cachexia as there is with carcinoma.

Diagnosis.—The rapidly growing tumor in the region of the kidneys, without much pain and the frequent renal hemorrhages, would indicate a sarcoma rather than a carcinoma.

Prognosis.—Here, as in carcinoma, it in all probability will prove fatal.

Treatment.—The only method of treatment which offers any prospect of recovery would be that of nephrectomy.   In the table of one hundred cases collected by Harris,[1] there were twelve which were either pure sarcoma, adeno- or angio-sarcoma; in 41.66% of these twelve, there was a complete recovery from this operation; in 33.33 per cent, death resulted; in the remaining 25 per cent, the diagnosis was doubtful, or the authenticity of recovery was uncertain.

Dividing the cases into two classes and making the best showing possible, 58.33 per cent recovered from, and 41.66 per cent died from the operation.

Dr. Weir records in all thirty-two cases,[2] in which this operation has been performed for various kinds of tumors of the kidneys, and finds the mortality to be 68.75 per cent.

From this high mortality he argues that the operation cannot be considered a surgical success, and remarks: "I think that the principal, if not the sole condition in a diseased kidney that justifies a nephrectomy is a suppurative process."

In Dr. Gross' paper upon nephrectomy, the following is found : "The kidney has been removed for sarcoma thirty-three times, with fourteen recoveries and nineteen deaths, or a mortality of 57.57 per cent.   In other words, 57.57 per cent died as the direct result of the operation, while of the survivors 42.85 per cent died subsequently,

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[1] Harris, R. P., "An Analytical Examination of One Hundred Cases; with a tabular record arranged chronologically." American Journal of the Medical Sciences, July, 1882, p. 109.

[2] Weir, Robert F., "Remarks on Extirpation of the Kidney, with Cases of Nephrectomy for Pyonephrosis, and Nephrotomy for Rupture of the Kidney." Medical News, Philadelphia, December 27th, 1884, p. 709.

and 35.71 per cent remained well for thirty-one and a half months on an average." [1]

CARCINOMA OF THE KIDNEYS.

Definition.—This is a condition in which the kidneys are the seat of an epithelial growth having the characteristic appearances of carcinoma.

Etiology.—The cause of this disease is not known. Primary cancer is said to be more frequent in the kidneys of children than adults.

Pathological Anatomy.—In primary carcinoma of the kidneys, the
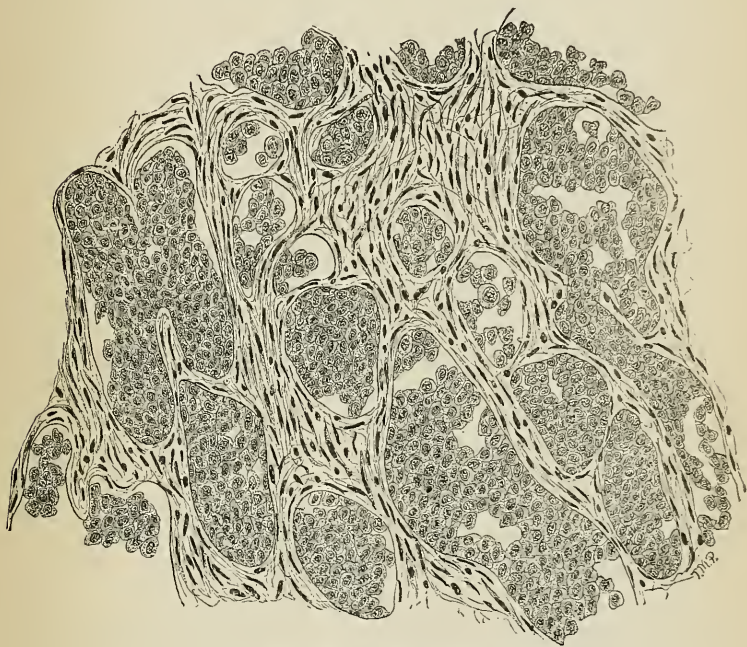
Fig. 32.—Medullary Carcinoma.
("Handbook of Pathological Anatomy and Histology," Delafield and Prudden.)

organs often become very large. The neoplasm may be twelve inches long by six inches broad (30.4×15.2 centimetres). It will weigh five or six times as much as a normal kidney. The shape of the gland is usually retained, but the newly formed tissue is most abundant in the cortical substance. The neoplasm may be evenly diffused throughout the organ, or it may be in localized nodules

[1] Gross, S. W., "Nephrectomy, its Indications and Contra-indications." American Journal of the Medical Sciences, Philadelphia, July, 1885, pp. 79, 85.

which are separated from each other by altered renal tissue. The calices and the pelvis are also invaded.

The renal substance immediately adjacent to these nodules will be found either in a state of atrophy or hypertrophy, with the formation of new connective tissue, depending upon the amount of pressure or irritation.

The renal epithelial cells undergo more or less of a fatty disintegration.

The blood-vessels are usually congested.

The exact method by which this neoplasm is developed in the kidneys has not been satisfactorily demonstrated.

Microscopic examination, as a rule, reveals the evidence of medullary carcinoma, in the shape of very thin and delicate alveolar walls, forming spaces the contents of which are composed of irregularly shaped nucleated epithelial corpuscles. These cells are packed into these alveolar cavities without reference to order of arrangement and without intercellular tissue.

The encephaloid is the variety most commonly found in the kidneys, but the colloid and other forms have been described.

Symptoms.—The leading symptoms are pain, localized in the region of the kidneys, associated with a rapidly growing tumor at the same point. The neoplasm may be smooth or nodular. The growth of a carcinoma at this point is more rapid than at any other portion of the body. This form of abdominal tumor is said to be the most frequent in children, and consequently the first to be thought of in case of abdominal distention. In adults the growth is also rapid.

There are usually recurring attacks of hæmaturia, with a variable interval between. After a short time, there is marked emaciation, with the characteristic cachexia.

Diagnosis.—The recurring attacks of hæmaturia have been considered diagnostic. Certainly, with the clinical history, and the rapidly growing and painful tumor, there ought not to be much doubt as to the nature of the disease.

Prognosis.—This is always fatal.

Treatment.—This also is palliative and not curative. Operative interference has been and may be resorted to, but as it offers so little prospect of relief, it is hardly warranted.

Gross, in speaking of the results of removal of the kidney for carcinomatous and sarcomatous growths together, says: "In 49 cases, 61.22 per cent die as a direct result of the procedure; that 16.32 per cent perish subsequently; that 12.24 per cent appear to make a permanent recovery." Subtracting the more favorable results obtained

in sarcoma alone, the success of carcinoma alone would be even more infrequent than the above figures would indicate. The lumbar operation appears to be less dangerous than the ventral.

ADENOMA OF THE KIDNEYS.

Definition.—Adenoma of the kidneys is that condition in which a neoplasm is developed in the substance of these organs, which offers the same structure as the racemose gland type.

Two varieties have been described, the papillary and the alveolar adenoma.

Etiology.—Of this little is known; probably the misplaced germ theory offers as satisfactory an explanation as any.

Pathological Anatomy.—Adenoma is equally frequent in both kidneys. They are most frequently located at one or the other extremity, rarely in the centre. They are commonly found in the cortical substance near the periphery; seldom in or near the pelvis. When close to the surface, the capsule also is involved. As a rule, they are single, but two or more have been recorded. Both kidneys are invaded in about twenty per cent of the cases; the size varies between that of a millet-seed and a hen's egg, or even larger; the more frequent size, however, being equal to a walnut or hazelnut. Their consistency is almost the same as the renal substance, unless they have undergone metamorphotic changes.

Papillary Adenoma.—When a papillary adenoma is completely developed in the kidneys, it is separated from the surrounding renal tissue by a capsule which varies in thickness. Within this capsule, there may be a single growth, or it may be divided into several compartments, each filled with papillary neoplasms. These grow out from one or more centres of the cavity wall, with a vascular network, sometimes abundant, and again deficient in round and spindle cells. When one or several growths are examined, they somewhat resemble a tree. The walls of the cavity are lined with a layer of epithelium, the cells of which have various forms and sizes, though the cylindrical epithelium is the type most frequently found. Not unfrequently the epithelial cells have undergone a fatty degeneration, and in some cases pigment granules are also found. In every case in which the tumor has several cavities, there is found between them a fibrous web of kidney substance. In the latter case, the uriniferous tubules are easily seen, variously compressed, or distended with colloid matter, while the Malpighian capsules have undergone fibrous degeneration, or are transformed into cysts. When more recent stages of papillary

adenoma are observed, however, it is seen that it is not limited by the surrounding renal tissue. It is made up of numerous cavities containing gland lobules which increase from the periphery toward the centre; the cells bearing a striking resemblance to the epithelium of the collecting tubes of the cortex. The lobules lie so close together that there is scarcely room between them for a firm connective-tissue stroma, though in some places there is quite a wide separation.

Alveolar Adenoma.—This is shown, as its name indicates, by an exquisite alveolar structure. The alveoli are of various sizes and shapes, the smallest being less than the cross section of a convoluted tubule. They are round, oval, cylindrical or irregular in shape, and contain epithelial-like cells, or there may be a central fissure or even a complete lumen. The cells have a peculiar character, being generally large, polyhedral, prismatic, or wedge-shaped, still free from retrograde metamorphosis, and lying in a homogeneous or granular protoplasm. Between the alveoli there is a very slight connective-tissue stroma which is structureless, or contains spindle-shaped cells, and in which the blood-vessels ramify. When the alveolar adenoma attains a certain size, like papillary adenoma, it becomes invested by a capsule. Whilst both the papillary and alveolar adenoma have clearly defined forms, and are easily recognized during their genesis, they so closely resemble each other in their latter stages that they can scarcely be distinguished.

These tumors are said frequently to undergo metamorphotic changes: 1, fatty; 2, fibroid; 3, fibrous; 4, cavernous and pigment metamorphosis; 5, cystic degeneration; and 6, colloid degeneration, with the formation of concretions in the stroma.[1]

Symptoms.—During life, when small, it is hardly to be expected that they would produce any symptoms that would attract special attention. There is, however, one case reported by Czerny, in which the left kidney was extirpated for a large adenoma of that organ in a child eleven months old.

Differential Diagnosis.—The diagnosis between adenoma and carcinoma is most important. Alveolar adenoma may easily be confounded with carcinoma, as not only the alveolar structure, but the cells resemble those of a carcinomatous tumor, the adenoma cells being scarcely less polymorphous than cancer cells. But after an adenomatous tumor has attained a certain size, it possesses a capsule, in which respect it differs from carcinoma. A careful microscopic examination, however, will decide the diagnosis.

Adenoma is diagnosed from fibro-sarcoma by the fact that the

[1] Medizin. Jahrbücher, 1883, Hft. ii.

latter occurs in old age, and only in the medullary substance of the kidneys, and by the well-known miscroscopic appearance of sarcoma. Adenoma is easily diagnosticated from hæmatangioma cavernosa, and from cystic disease of the kidneys, by the macroscopic and microscopic appearances.

FIBROMA OF THE KIDNEYS.

Localized and dense masses of white fibrillated connective tissue have been found in the outer portion of the medullary substance. They are usually considered as localized patches of interstitial nephritis. This appears to be the nearest approach that occurs to a fibrous neoplasm in the kidneys.

CONGENITAL RHABDO-SARCOMA OF THE KIDNEYS.

A congenital striped-muscle sarcoma has been described in Virchow's *Archives*, Bd. LXV. The kidneys were removed from a child who had been healthy during the first year after birth. At this time it sickened, and three months later died.

Both renal organs were invaded by tumors, which were found, on microscopic examination, to be composed of striped muscle fibres. The fibrillæ were small, long, and interwoven. A sarcolemma was not discovered. In other parts, but not so plentifully, the typical structure of sarcoma was found. It was explained, according to Cohnheim, by an original faulty growth, and not as a result of metastasis.

ANGIOMA OR CAVERNOUS TUMORS OF THE KIDNEYS.

In rare instances, a neoplasm has been found in the kidneys, composed of a bunch of dilated capillaries, and closely resembling erectile tissue. They are analogous to the cavernous tumors so frequently found in the liver. In size they vary from a small pea to that of a hickory nut. These formations are pathological curiosities only, having no clinical significance.

LIPOMA OF THE KIDNEYS.

Lipoma of the kidneys is another rare form of neoplasm. Two tumors of this character have been found in making about one thousand necropsies. This would make its frequency one in five hundred.

In the first case, the neoplasm was located in the medullary portion of the kidney; it was about one inch (2.5 centimetres) in diameter. The new growth was surrounded by a distinct capsule, and from its

macroscopic appearances might easily be mistaken for a medullary carcinoma or a round-celled sarcoma. But an examination by the microscope proved conclusively that it was composed of adipose tissue. In the second case, the neoplasm had its origin in the cortex, about one-fourth being imbedded in the renal tissue, the remaining three-fourths protruding beyond the free surface of the gland. In this instance, the new growth was distinctly encapsulated and lobulated ; upon microscopic examination, it was found to be composed exclusively of adipose tissue.
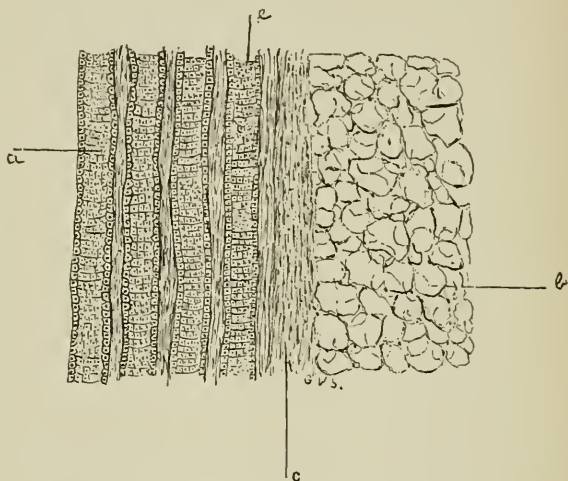
FIG. 33.—LIPOMA OF KIDNEY. × 350.

a, Straight collecting uriniferous tubules ; b, lipoma imbedded in the kidney tissue ; c, fibrillated connective-tissue capsule of the lipoma ; e, commencing parenchymatous metamorphosis of the renal epithelium.

This second tumor was about one and one-half inch (7 centimetres) long by one-half inch (2.3 centimetres) in thickness.

LYMPHOMATA OR LEUKÆMIC TUMORS.

Lymphomata or leukæmic formations have been found in the kidneys. This is a condition in which one or more small neoplasms, varying in size from a small dot to that of a cherry, are found. In shape they are round, pyramidal, or oval, and composed chiefly of lymphoid corpuscles in a delicate adenoid reticulum. From the frequency with which Virchow and Rindfleisch found a collection of red blood-discs in their centre, they were led to believe that these neoplasms had origin in an extravasation.

Such neoplasms are of pathological rather than of clinical interest.

OSSEOUS TUMORS.

Bony transformation of a fibrous thickening has been recorded in a few instances.

GUMMATA OF THE KIDNEYS.

Syphilitic disease of the kidneys in the shape of gummy formations, although not common, is more frequent than has heretofore been supposed. Gummata of the kidneys are usually small and multiple, and are most frequently located in the cortical portion. Here, as in other parts of the body, they are pale, granular-looking deposits, often having a cheesy centre. But the periphery is a little more distinct, and frequently is formed of concentric layers of incompletely fibrillated connective tissue, containing small blood-vessels, thickened by a hyaline metamorphosis. By this tendency to encapsulation and the peculiar thickening of the blood-vessels, their nature can be determined.

A special syphilitic disease of the kidneys, without gummata, in which there is an interstitial thickening and amyloid transformation, characterized by albuminuria, etc., has been described.

Such a disease is here omitted, as the various forms already described are believed to completely cover the question, and also from the fact that syphilis *per se* seldom excites an acute renal lesion. It is very uncommon to meet a case of acute renal disease during the active symptoms of syphilis, and when it does occur, it is a question as to the excitant, whether it is the syphilis, the medicines used, or some extraneous cause. On the other hand, from an extended clinical macroscopic and microscopic study in well authenticated cases of syphilis, the firm conviction has been developed that the syphilitic vice determines in a large measure whether the force of the renal disease is to be spent upon the interstitial tissue, blood-vessels, or epithelial cells.

In patients suffering with a specific taint, a peculiar hyaline transformation and thickening of the blood-vessels is found, which appears to be diagnostic of the syphilitic disease, and which does not exist where syphilis is not present.

When a renal lesion is developed in a person with a specific taint, unless directly referable to the causes for the parenchymatous group, it is most likely to be of the chronic diffuse variety with vascular changes; or of a cirrhotic or an amyloid form. Observation in several necropsies where there had been long-continued suppuration of the bones with an absence of a syphilitic vice and of the amyloid or hyaline changes in any part of the body, has developed

the belief that the syphilis is always the essential factor in producing this hyaline vascular change; it was always marked in those cases in which a decided specific taint was certain.

The oft reiterated remark that small and repeated doses of the bichloride of mercury and iodide of potassium do as much, if not more good than all other medicinal agents in Bright's, certainly aids in substantiating the above view. Why not say, as syphilis is a frequent etiological factor in producing, not only renal diseases, but many other visceral lesions, that it should always be sought after and treated ? The almost universal occurrence of syphilis is not a pleasant topic from the moral side of the question, but from the medicinal it is, for if the cause of the disease can be traced to a latent syphilis, and is early recognized as such and properly treated, recovery will result, where otherwise death would ensue. Who would not grasp at life, even with a syphilitic taint, against a certain death warrant ?

CHAPTER XV.

PARASITES: ECHINOCOCCUS, BILHARZIA HÆMATOBIA, STRONGYLUS SEU ESTRONGYLUS GIGAS, ASCARIS RENALIS.

HYDATIDS OF THE KIDNEYS.

ECHINOCOCCUS CYSTS.

Definition.—The hydatid or echinococcus cyst is that form of disease in which an immature embryo of the Tænia echinococcus finds its way into the kidney, and becomes fixed and swollen to a large vesicle, on the inner wall of which a colony of young and immature scolices is developed.

Etiology.—Hydatids are always due to the ingestion of the eggs of the Tænia echinococcus, which may be taken in either with the water or food.
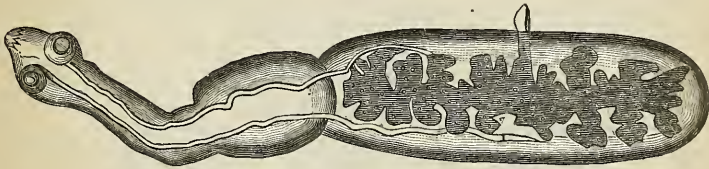
FIG. 34.—TÆNIA ECHINOCOCCUS COMPLETE. × about 16.

The formation of the hydatid cyst is almost always a slow process.

Their frequency depends upon the abundance of dogs and the habits of the people. They are quite common in Iceland, Egypt, and in South Australia. In other countries they are exceedingly rare.

Pathological Anatomy.—The hydatid may be one of three varieties: exogenous, endogenous, or multilocular. The first is rare in man; the second and last, especially the endogenous, are found in the human subject.

The essential character of the growth is the formation around the parasite of a tough and well-developed capsule, composed of fibrillated

connective tissue, from which other bands of connective tissue pass into and across the cyst cavity in every direction, thus forming small interstices.

The alveoli are of various sizes and shapes, lined with vesicles and filled with gelatiniform plasma, and occasionally with the so-called echinococcus heads. A few blood-vessels may be found ramifying through the mass, but no glandular tissue.

FIG. 35.—CUTICULA OF ECHINOCOCCUS CYST. × 250.

(" Handbook of Pathological Anatomy and Histology." Delafield and Prudden.)

From without inward we find first an investing capsule, formed from the surrounding tissue. Within this there is a thick, homogeneous laminated elastic membrane which, when withdrawn, displays a peculiar tremulous motion and coils upon itself when cut. This is the so-called cuticular structureless layer, or *entocyst* of Huxley. Within and closely applied to it, lies the *endocyst*, of the same author. This
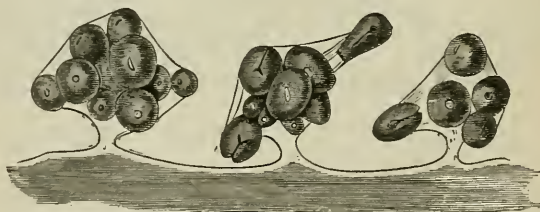
FIG. 36.—ENDOCYST OF HUXLEY, SHOWING BUDS AND GEMMÆ.

is a thin, soft, comparatively non-elastic, granulated membrane and forms the essentially vital part of the bladder-worm. From this inner membrane buds are produced and these gemmæ become transformed into echinococcus heads, both directly and indirectly. The brood capsules often contain many heads, and by a process of eversion project into the general cavity of the mother hydatids. By

a process of proliferation, daughter and grand-daughter hydatids are developed within the maternal cyst, and these smaller cysts also produce the heads. Beyond this point, their method of development is uncertain, and just how the heads are formed is unknown.

When located in the kidney, the organ becomes enlarged, sometimes to an enormous extent. The cyst may connect itself to neighboring organs by inflammatory adhesion. A globular tumor projects from the surface and is imbedded in the kidney. By its pressure it often induces atrophy of the renal tissue. The cyst has for an outer covering a fibrous capsule of its own. The hydatid may be barren, that is, free from daughter cysts, or it may be made up of many smaller cysts, and processes growing inward and containing scolices, which may give origin, if taken into the proper system, to the corresponding tapeworm in that animal. In either case, the cyst-wall is tensely expanded by a clear liquid, rich in the chloride of sodium.

FIG. 37.—SCOLICES OF TÆNIA EHINOCOCCUS. × 60.

In one the rostellum is projected, in the others it is withdrawn. (Delafield and Prudden, "Handbook of Pathological Anatomy and Histology.")

The cysts enlarge gradually and burst in various directions, either into the pelvis of the kidney, lung, bronchi, peritoneum, etc., but most frequently into the renal pelvis.

The hydatid may suppurate and the necropsy will show the remains only of a shrunken and shrivelled cyst, with its cheesy contents, in which are imbedded the remains of the daughter-cyst and hooklets.

Symptoms.—The course of hydatids in the kidneys is slow and chronic, often lasting for many years. The first evidence of their existence may be the discovery of a tumor, or rupture may be the first indication. This may occur with or without a previous discovery of the tumor.

If the sac ruptures into the renal pelvis, the passage of the daughter-

cyst through the ureter may give rise to all the symptoms of renal colic.

The finding of the remains of the cyst or the hooklets in the urine will complete the diagnosis.

The ruptured cyst may collapse and atrophy. Two or more discharges may occur from the same cyst at varying intervals.

If they open and discharge by the respiratory tract, thoracic pain and cough will be the prominent symptoms. Remnants or hooklets will be found in the sputum. Such cases terminate quite favorably.

The globular form and elastic nature of the tumor strongly favor the presence of hydatids. If the cyst suppurates, local pain and fever are the additional and prominent symptoms.

Diagnosis.—The peculiar form and elasticity of the tumor is strongly indicative of its being of hydatid formation. Finding cysts and hooklets in the urine, or in the fluid withdrawn by aspiration, confirms the diagnosis.

Prognosis.—This is very uncertain; nothing positive can be given.
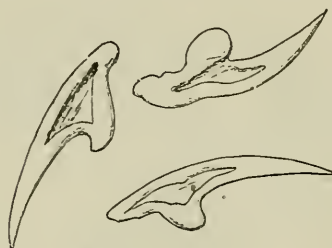
FIG. 38.—HOOKLETS FROM SCOLEX OF TÆNIA ECHINOCOCCUS. × 750.

(Delafield and Prudden, " Handbook of Pathological Anatomy and Histology.")

Treatment.—Medical agents are useless. The fluid may be removed by aspiration, when the parasite will frequently die and the cyst shrivel and become obliterated. Oil of turpentine has been administered, also male fern, but their utility is doubtful.

The radical treatment is surgical. Both electrolysis and nephrectomy have been employed with good success.

BILHARZIA HÆMATOBIA.

Definition.—This is a peculiar parasite, found in certain localities in Africa and Europe, which, when taken into the system, becomes lodged in the urinary apparatus and gives rise to an epidemic hæmaturia.

Etiology.—This name was given to this special entozoon by Professor Cobbold in 1851, from the fact that Dr. Bilharz was the first to

discover the parasite. The worm was first found in the portal vein of a man, next in the same vein of a monkey. At first it was supposed to be a *Distoma,* but it is now generally known as the *Bilharzia hæmatobia.* Later, the same parasite was found in the mesenteric and vesical veins, and also in other parts of the body, producing symptoms of a formidable disease. Finally, it was found in the urine.

Dr. John Harley next discovered that a form of epidemic hæmaturia at the Cape of Good Hope was due to a parasite which he considered a new species. Further research, however, proved that it was the same Bilharzia, and this latter conclusion is now pretty generally accepted. The researches of Dr. Harley were very important,
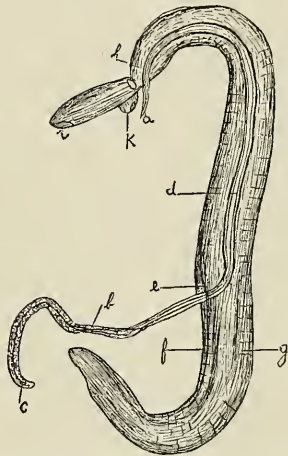
Fig. 39.—Bilharzia Hæmatobia. × about 15 times.

a, b and *c,* The female, partly placed in the gynæcophorous canal of the male; *a,* anterior extremity; *c,* posterior extremity; *d,* body seen within the canal; *e, f, g, h* and *i,* the male; *e, f,* gynæcophorous canal, from which the female has been partly extracted; *i,* buccal sucker; *k,* ventral sucker; between *i* and *k,* the trunk; after *k,* the tail. After Bilharz.

however, as they showed a much greater geographical range for this parasitic disease.

Pathological Anatomy.—These worms differ from all the other varieties of flukes in having separate sexes.

The female is a very slender worm, resembling filaria-form nematoids. During copulation, the female is lodged in a long slit-like groove or gynæcophoric canal with which the male is furnished. The ova measure from $\frac{1}{180}$ to $\frac{1}{60}$ of an inch (1.4110 mm. to 4.233 mm.),

11

and are sharply pointed at one end. They are a form of ciliated embryo, a complete and extended description of which will be found by Dr. Cobbold in the *British Medical Journal*, 1872.

Both the male and the female are found lodged in the walls of the human bladder.

Symptoms.—There are no characteristic manifestations at first, and, as a rule, there is no evidence of the entozoon having become lodged in the human system, until it has matured and commenced the discharge of ova. The first symptom is pain on passing water, and at the end of micturition there is a discharge of a few drops or more of blood.

Microscopic examination of this bloody urine will reveal the presence of the fertilized ova, and this will render the diagnosis positive.

There is little or no general distress; but in some cases there may be a dull aching sensation in the lumbar region. But in the more aggravated cases the bleeding increases until the quantity of blood lost at each micturition is considerable, not alone mixed with the urine, but in some instances clots are also expelled. Now there is severe perineal and lumbar pain, and a vesical catarrh is developed which is not easily relieved, as its cause cannot be removed.

Diagnosis.—Persistent hæmaturia, in those sections of country where the entozoon is known to exist, and the finding of the ova in the bloody urine, settle the question beyond a doubt.

Prognosis.—It is usually good. Dr. Vasy Lyle makes the following statements: " Grave as the picture is, I must, however, state that I have not met with a fatal case of *Bilharzia hæmatobia*, whether arising directly or indirectly from the presence of that entozoon." But in the severe cases it may be several years before a complete cure is effected.

Treatment.—Dr. Cobbold considers it unwise to employ active drugs with the view of expulsion, or vermicides with a view to destroying the parasite, as both do more injury than good.

The system, on the contrary, needs to be supported and given strength to withstand and arrest the hæmorrhages, and eventually rid itself of the worms.

The arctostaphylos uva ursi, either alone or combined with hyoscyamus, has been found the most serviceable in forming a barrier around the entozoon and in preventing the hæmorrhages. At the same time the patient should be ordered tonics, cold bathing, and the most nutritious diet, and if possible be removed from the locality where he is supposed to have contracted the disease.

Diuretics and vesical irritants of all kinds are contra-indicated, the reverse being more efficacious.

STRONGYLUS SEU ESTRONGYLUS GIGAS.

ASCARIS RENALIS.

Definition.—This parasite is a round worm of the genus Ascaris.

Etiology.—This entozoon has been found in man, horses, oxen, hogs, mules, wolves, and fish-eating carnivora.

It is much more common in the lower animals than in man; only a few cases having been recorded in the human subject.

Pathological Anatomy.—In a necropsy made upon a horse which had been infected by this parasite, the following conditions were found, and are given in detail :

The peritoneal cavity contained a large amount of blood and coagulum, also about twenty of these round worms, varying in length from $3\frac{1}{2}$ to 8 inches (9.989 to 20.319 centimetres).
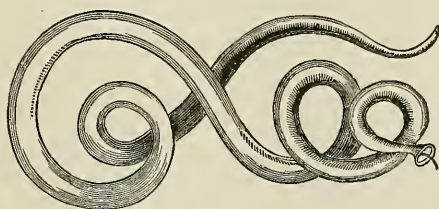
FIG. 40.—STRONGYLUS SEU ESTRONGYLUS GIGAS.

The genito-urinary tract up to the kidneys appeared to be normal, but both these glands were the seat of very interesting changes, and presented a very peculiar appearance. They were full of small round holes, about one centimetre (two-fifths of an inch) in diameter. These canals were very numerous, and gave the kidneys a worm-eaten appearance.

For two reasons this change was supposed to be due to the passage of these round worms through the tissue of the glands. *First,* the holes passed through the renal capsule, as well as the kidney tissue ; and, *second,* a worm was found in one of the kidneys, and protruded from one of the holes at the time of the necropsy.

Microscopic examination of the organs showed the renal epithelial corpuscles to be slightly granular, but otherwise quite normal in appearance. Transverse sections of the openings gave them the appearance of pretty clear-cut holes, at the expense of the renal substance.

Each canal was surrounded by a thin layer of inflammatory exudation, but this action was limited to a very thin area, and evidently had not irritated the gland tissue to any marked degree.

A similar, if not the same, form of strongylus has been reported as occurring in the kidneys of the mule by Dr. Ballinger, of Cincinnati. In his cases, some of the kidneys were entirely destroyed and replaced by a ball of these worms.

The parasite itself has been described as a slender, cylindrical worm, from two to six inches in length, and of a light gray color. In some they have made their way into the parenchyma of the organs, and caused suppuration, atrophy, and other mischief.

The male strongylus is smaller than the female, and tapers slightly towards each extremity. The head is obtuse, and furnished with an orbicular mouth, encircled by six hemispherical papillæ; the body, transversely striated, is marked by two longitudinal impressions; and the tail, which is incurvated, ends in a dilated pouch, from the base of which a penis projects. In the female, the tail is less pointed than in the male, with the anus just below the apex; the vulva is situated a short distance from the head, and communicates with a slender cylindrical vagina ; the uterus in the large individuals is about three inches long, and leads to a simple ovary, nearly four times the length of the body. The nervous system of the body consists of two delicate rings, one encircling the œsophagus, and the other the anus, and connected by a single cord extending along the middle line of the belly.

Symptoms.—Too few cases have been recorded to yield any trustworty data. They are, when found in the human kidneys, rare curiosities. When present, they are said to cause much distress. A clinic patient once related the passage of a number of worms with the urine, corresponding to this description, but at the time little attention was paid to the narrative, as none of the parasites were preserved. The story may, however, have been true, and and may have been a case of this kind.

Treatment.—For the expulsion of these worms, turpentine, cubebs, and copaiba have been advised.

CHAPTER XVI.

GLYCOSURIA OR DIABETES MELLITUS.

ITS ETIOLOGY, PATHOLOGY, CLINICAL HISTORY, AND TREATMENT.

Definition.—This is a disease in which no uniform lesion has here-tofore been described, but in which there is a constant and primary parenchymatous metamorphosis of the hepatic cells, followed by a similar metamorphotic change in the epithelial corpuscles of the kidneys. Careful study of the microscopic changes in several cases where the patients died of this malady, lead to this decision, and the detailed account of three necropsies will constitute the pathology of this chapter.

The clinical features are drawn from a large number of cases which have come under observation, and which are characterized by the voiding of large quantities of urine, usually of a high specific gravity and more or less heavily loaded with glucose. There is also an abnormal craving for starches and sugars; great thirst, and, usually, progressive emaciation and weakness, all of which are characteristic of the disease. Numerous other symptoms due to secondary and complicating lesions are developed.

Etiology.—An inherited tendency to diabetes mellitus seems to be pretty clearly established in about twenty-five per cent of the cases. By some observers it is believed to be still more frequent, but, owing to the incomplete knowledge of the patient in regard to the disease of which their ancestry died, it is impossible to arrive at any positive conclusion.

Age.—The period of life is also important. The recorded observations show that it may develop at any time from birth to very advanced years. By dividing life into decades, commencing at birth, the combined results, as computed from the tables of Griesinger, Seegen, Schwartz, Andral and Mayer, show a progressive increase in frequency up to the decade included between forty-one and fifty, where it attains its maximum of frequency and continues stationary during the succeeding decade of fifty-one to sixty. The largest number,

therefore, may be said to occur between the ages of forty-one and sixty. The next frequent period is between thirty-one and forty; then between twenty-one and thirty; about an equal number occur between eleven and twenty, and sixty-one and seventy.

More recent observation and an earlier recognition of the malady is tending to increase the frequency of its occurrence in children and early adult life.

Sex.—The disease is generally spoken of as being more frequent in adult males; the proportion being about two to one. In children, the preponderance is in favor of the female sex.

The preponderance, among cases personally observed, in hospital and private practice, was, even among adults, in favor of the females, but, when the same number of each was taken as the standard of comparison, it was found to be of about equal frequency in both sexes. Of the forty cases, however, recorded by Prof. Satterthwaite,[1] twenty-seven were males, and thirteen were females.

Frequency.—This has been variously stated as ranging from one in six thousand to three in ten thousand, but if all the cases were detected and accurately recorded, it would probably be found as frequently as two in three thousand.

Ascribed Causes.—Under this division may be mentioned: alcohol in excess, mental anxiety, concussion of the spine, sexual abuse, opium, syphilis, mechanical injury, a variety of diseases and lesions of the nervous centres, especially in and around the medulla oblongata, physical impressions, pregnancy, tape-worm, etc., but the very diversity of these theories proves that no very definite idea exists of the real causation.

The most frequent predisposing and exciting cause, however, appears to be a super-nutrition of the portal system, which, with a parenchymatous metamorphotic change in the hepatic cells, is the primary lesion; the nervous involvement being peripheral, reflex, and secondary. It may be that over-mental activity, by weakening the nervous mechanism of the liver, allows that organ to give way under the increased pressure. This view is in a measure substantiated by physiological experiments which point toward increased nutrition as the essential to traumatic glycosuria.

Clinical experience teaches the same thing, namely, a greater frequency of this disease among the well-to-do classes, and in a large proportion of cases a careful inquiry into the habits of the individual shows an inordinate use of the starches, fats, and nutritive materials in general.

[1] New York Medical Record, April 11th, 1885, p. 396.

Pathologically the only positive lesions, as far as known, are to be found in the liver and kidneys.

Treatment also aids in sustaining the super-nutrition theory, for it is a well-known clinical fact that a nitrogenous diet, aided by such medicinal agents as steady both the nervous and circulatory systems, especially the latter, affords the greatest relief.

Physiological and Pathological Considerations.—Diabetes mellitus is said to be most frequent in the higher stations of life or among the well-to-do class of people. It is a noticeable fact that diabetes is especially frequent among the Jewish race, and strikingly so in wealthy Jewesses. Consequently it would appear that excesses—and by this is meant a physiological increase in nutritive material, which tends to keep the liver or hepatic cells continually overworked—should be considered the starting-point. This condition may result from eating too freely of hydro-carbonaceous substances, either alone or in conjunction with the proteids, both of which materially impair the physiological activity of the hepatic cells, and thus excite a condition which renders them incapable of performing their normal work. Overcharging the portal blood with glucose or cane-sugar has been found, by actual experiment, to be followed by glycosuria.

The experiments of Pavy show that oxygenated blood injected into the portal circulation produces a super-oxygenation which apparently increases the amount of work on the part of the liver, and which is followed by glucose in the urine. A number of similar experiments could be cited, besides those of Schiff, who excited glycosuria by direct galvanization of the hepatic substance, as a proof that the primary trouble was located in the liver; but Pavy's experiment and the introduction of sugar into the portal blood appear to point more directly to the solution of the mystery.

From these observations it seems reasonable to suppose that an excessive imbibition of nutritive elements into the portal circulation must, of necessity, call for a super-oxygenation of the portal blood; thus throwing additional work upon the hepatic cells; in consequence of which the capillaries are dilated to furnish the necessary material to carry on the excessive metabolism, and this peculiar disease is developed by natural as well as experimental processes. It may be that this increased demand which is made upon the liver is transmitted through the sensory filaments of the sympathetic system, to the hepatic medullary centre, producing either deficient or excessive stimulation as the case may be, which, when it is transmitted back to the liver, leads to an incomplete function, or an undue activ-

ity on its part, instead of the exact equilibrium which should be sustained.

This theory is quite as much in keeping with physiological laws as the attempts to trace its source to indefinite and varying cerebral lesions, which, in many cases, are wholly absent. Not that cerebral lesions may not interfere with the nervous mechanism of the liver, bring about this change in the capillaries and hepatic cells, and result in incomplete or excessive transformation. In traumatic diabetes the tendency is to recovery, which, as in experimental diabetes, proves the necessity of a surcharging of the portal system with nutritive materials to produce the permanent disease. In proof of this view may be cited limitation, if not absolute restriction, of the diet, with a regulation of the vascular system, which, in many cases, causes a marked diminution of the glucose in the urine, and in some its total disappearance, while a neglect to observe these laws almost invariably increases the quantity.

The case recorded by Brunton serves as a proof of these statements, since here, the glycosuria was directly traceable to the irritation caused by a tape-worm. Undoubtedly the primary disturbance of the nervous system, in this instance, was produced by the irritation of the peripheral sensory fibres of the sympathetics, which conveyed the impression to the medulla, whence it was transmitted to the liver. The removal of the parasite was almost immediately followed by a permanent disappearance of the sugar.

It might be, however, that the enormous appetite which is sometimes produced by a tænia was the cause of surcharging the portal system with nutritive material, and of thus producing the disease. In either case, the nervous irritation was peripheral and not central.

The frequent occurrence of temporary glycosuria in pregnancy is explained by the utero-gestation causing the well-known peripheral irritation of the sympathetic system, and throwing more work upon the liver; the same irritation exists during lactation, but is especially marked when, for any reason, the flow of milk is suddenly arrested, causing increased peripheral irritability of the nervous system, and at the same time throwing more work upon the liver. This explains the glycosuria which occurs in both these instances, and helps to sustain the present theory of increased nutrition, an hepatic lesion, and peripheral nerve-irritation.

The weight of evidence, deduced from the large number of experimental and pathological lesions of the nervous system, points decidedly in one direction—namely, that to produce glycosuria, even tem-

porary in nature, there must be an increased amount of nutritive material in the blood of the portal vein.

The frequency of the renal lesion in diabetes, which is an epithelial metamorphosis of a peculiar and severe type, and the finding of no evidence of sugar in the blood, in many cases, as was practically proven by a recent necropsy, suggest the probability that glucose is not produced by the liver, or discharged as such into the blood. The liver, however, does produce the *sugar-forming elements* which circulate in the blood until they are conveyed to the kidneys, where they are seized upon by the renal epithelial cells as foreign substances, drawn from the circulation, changed into glucose, and discharged into the uriniferous tubules. Admitting that all forms of parenchymatous metamorphoses of the kidneys are due to an increased amount of work on the part of the renal cells, this explanation offers a tangible reason for the very general if not constant renal lesion found in these cases. It also helps to explain the final termination of so many by a kidney lesion, which is usually indicated by albumin and casts. The small amount of albumin may be explained upon the theory that some, if not a considerable quantity, of the glucose is produced from the albuminoids, and that the sugar represents what otherwise would be eliminated as albumin, urea, carbon dioxide, and water.

Exception may be taken to this view from the fact that sugar has been said to have been found in the blood of a diabetic patient during life; but both urea and sugar are said to be found in normal blood; yet there does not appear to be a sufficient quantity of sugar present to account for the large amounts discharged in the urine. In regard to urea, this statement is known to be the fact.

The close relationship existing between the sympathetic nerves of the liver and those of the kidneys explains the primary dilatations of the renal vessels. The marked increase in the lumen is maintained by the hyaline transformation, which causes a permanent thickening of the vascular wall and completely destroys its elasticity. The result of this is that all power to regulate the pressure upon the glomeruli is removed, and the increased hydrostatic pressure forces a very large quantity of water through, which explains the copious quantity of urine voided.

The *pathological anatomy* of diabetes as here given is based upon a number of necropsies, in all of which a marked parenchymatous metamorphosis of the liver and kidneys was the chief lesion. Three are given in full to illustrate the characteristic, as well as some of the accessory changes. Usually after wasting diseases of any duration, the cadaver is found much emaciated, but in some instances, when

they die early, the body may retain its rotundity. In two of the cases cited, there was marked emaciation; one, however, died in what might be called full flesh, even though the disease had lasted for more than a year.

The following is the result of the necropsy in full, with two others appended, together with all the various lesions that have been described as being found by different observers.

Rigor mortis was absent, the lower extremities were covered by an eruption which did not disappear upon pressure. This was syphilitic in all probability. The skin was unusually pale and blanched. The panniculus adiposus was nearly absent. The muscles were thin and dry. The pericardial sac contained about half an ounce (15.5 c.c.) of clear
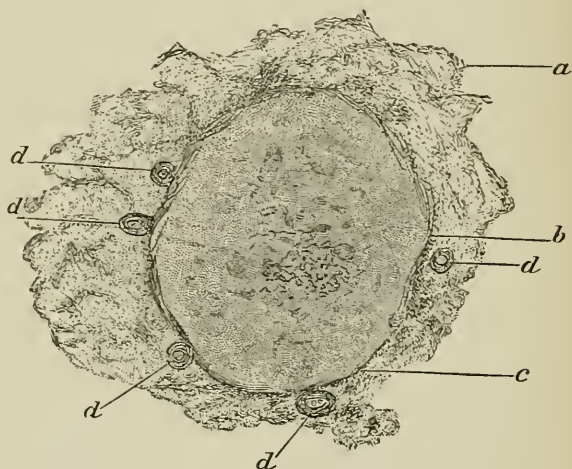
FIG. 41.—MILIARY GUMMA.

Showing cheesy centre, fibrillated capsule, and hyaline thickening of capillary vessels. *a*, Surrounding pulmonary substance; *b*, *c*, fibrillated connective-tissue capsule walling in cheesy centre; *d*, hyaline metamorphotic thickening of the capillary blood-vessels.

serous fluid. The heart cavities contained a small quantity of blood and coagulum. The muscular tunic was very soft and flabby, so that the cavities collapsed and the organ became flattened when it was laid upon the table. Microscopic examination showed granular and fatty degeneration of the cardiac muscles. All the valves were free and sufficient, but, owing to the relaxed condition of the organ, could not be made to close perfectly to the water-test. The heart weighed eleven ounces (311.844 grams).

In the other two, the heart was slightly enlarged, in the third case weighing nineteen ounces (538.642 grams). In the second case, there

was some fatty infiltration. The muscular elements in it and the third case were similar to those described in the first. There was marked fatty infiltration of the valves on the left side of the heart in all, and of the aorta in the second and third cases.

The left lung was perfectly free in the pleural cavity. It presented nothing especially abnormal. There was, however, a slight amount of interstial thickening of the apex and the superior portion of the upper lobe. It weighed twenty-one ounces (595.340 grams).

The right lung was quite adherent at the apex, at which point the pulmonary tissue was indurated and presented the gross appearance
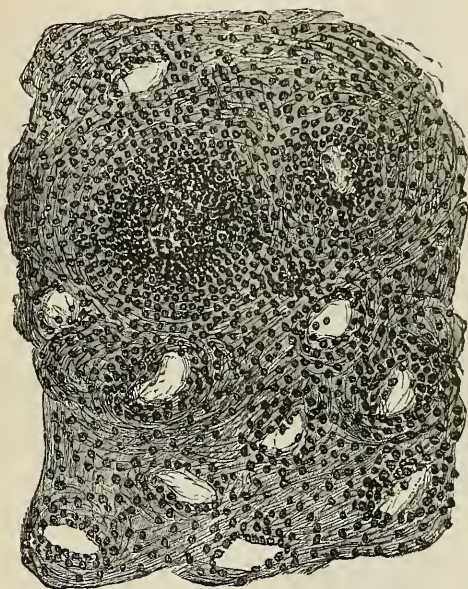
FIG. 42.—LARGE GUMMA.

Showing the outer portion and cellular infiltration; the open spaces representing spots of softening.

of consolidation, with a tendency to the formation of cavities. The remaining portions were free in the pleural cavity. When the indurated apex was bisected, a large, cheesy-looking nodule was divided, also numerous smaller zones of like material. Two small cavities were developing. The intervening pulmonary tissue was indurated. The contents of the cheesy nodule were examined for the bacilli of tuberculosis by Dr. G. R. Elliott, but none were found. The larger of the two distinct cheesy masses had the sticky feeling so common to gummy tumors. On microscopic examination, it appeared to be

partially encapsulated or blended with the adjacent pulmonary tissue
by a fibrous band, which was lined by concentric rings of fibrillated
connective tissue. The centre of this neoplasm was more decidedly
granular and cheesy. The surrounding pulmonary substance showed
to the unaided eye a distinct increase in connective tissue studded
with numerous granular spots or bodies somewhat resembling miliary
tubercles, but which proved to be miliary gummata, see Fig. 41.
Sections were made which included the capsule of this large mass and
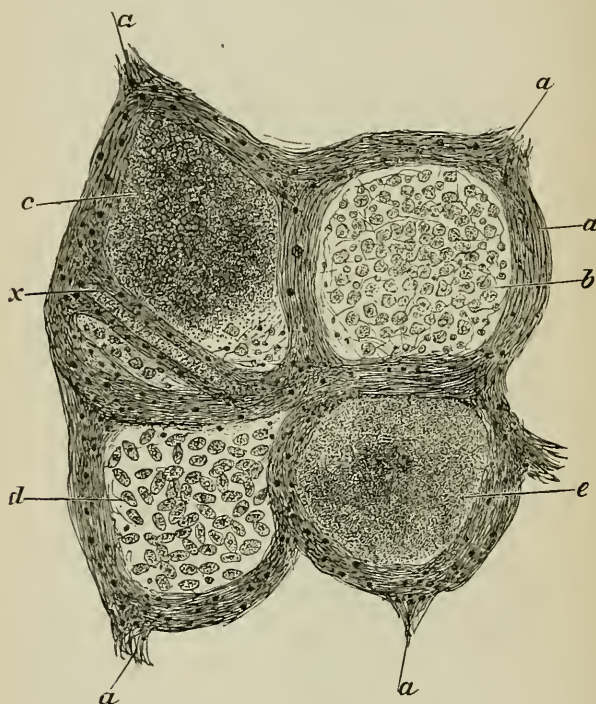
FIG. 43.—SYPHILITIC PNEUMONIA.

a, Thickened vesicular walls; *v*, an air-space showing red hepatization; *c*, an air-space show-
ing gray hepatization; *d*, an air-space showing catarrhal desquamation of epithelial cells; *e*, an
air-space showing the degenerative pneumonia of syphilis; *x*, a blood-vessel between two thick
bands of fibrillated vesicular wall.

the adjacent tissues on both sides. This apparent fibrillated capsule,
when examined under the microscope, was found to be composed of
numerous layers of fibrillated connective tissue which were irregularly
interpersed with blood-vessels.

Some of the tissue appeared to be of recent formation, in a state of

activity, and took the stain deeply, while other portions were older, granular and degenerated, and did not stain. On the inner side of this band, going toward the centre of the focus, the granular and degenerated condition became more and more decided. The structure closely adjacent to the outer portion was the vesicular tissue, but this was markedly altered. The walls of the air vessels were enormously thickened, being in some instances five or six times greater than normal, Fig. 43, *a*. Sections from various portions of this indurated nodule showed numerous broad bands of fibrillated connective tissue in various stages of formation. In some places they presented the lively and deeply stained appearance of newly formed connective tissue; at other points they appeared to be in a state of active inflammation, being dotted with deeply stained leucocytes; in still others they were almost obliterated by an abundance of deeply stained, round connective-tissue corpuscles, with positive nuclei, and of about twice the size of the lymphoid corpuscles. The last-described, if viewed alone, could not be distinguished from a round-cell sarcoma. See Fig. 42. Some of the fibrillated bands showed a slight disposition or carbon pigmentation. The yellow elastic fibres were very distinct and abundant.

In all the sections there was an unusual and marked thickening of the alveolar walls, which in many places were congested and in many others quite granular. See Fig. 43, *a*.

Numerous spots were found which somewhat resembled tubercle granulation, but close inspection failed to reveal any distinct tubercle tissue or giant cells with multiple nuclei. These zones were composed of this thickened tissue, and showed various changes in the alveoli, some of which were simply filled with red blood-corpuscles, some with fibrillated fibrin, red blood-corpuscles, and large and small desquamated epithelial or lining cells of the air-vescicles, Fig. 43, *b*. Some were simply packed full of these desquamated corpuscles, Fig. 43, *d;* others were filled with a granular substance which would not take the stain, Fig. 43, *e*. All these conditions were interspersed without any reference to a uniform progressive development of pneumonic inflammations. The walls of the capillary vessels were thickened, Fig. 43, *x*.

The interstitial induration diminished progressively from the apex to the base. The weight of the right lung was twenty-eight ounces (793.787 grams). Both lungs were slightly congested and œdematous, but no more than would be expected in connection with a death without special pulmonary symptoms.

This condition undoubtedly was that of a gummatous formation, rapidly approaching liquefaction and the formation of cavities. (See

Fig. 42.) The numerous smaller foci were probably smaller gummata, or the nuclei of larger ones. The interstitial thickening was of syphilitic origin (Fig. 43, *a*), which condition is quite frequent and often mistaken, clinically, for tubercular phthisis. This certainly was not a tubercular process.

In the second case, the lungs were normal, a slight amount of emphysema excepted.

In the third case, there was a marked destruction of the pulmonary substance, with the formation of large cavities. Their gross appearance was not that of a tubercular or syphilitic lesion, but was more that of an inflammatory and necrotic condition. Various portions of both lungs were subjected to both Erlach's method for staining the bacilli of tuberculosis and to Lustgarten's method for staining the bacilli of syphilis. In the former case, no blue bacilli were found, but with the latter they were quite numerous. If this be a differential test which can be relied upon, the lesion of the lungs in the third case was, like the first, syphilitic. These conditions of the lungs were of great importance. They established positively in the first case, and probably in the third, that the pulmonary affection was not tubercular, but syphilitic in origin.

It certainly suggests the inference that many reputed tubercular processes in the lung may have been due to a similar or independent condition.

Various lesions have been described as affecting the lungs in diabetic cases, particularly chronic inflammatory conditions leading to the formation of cavities; also all forms of pneumonia and tubercle with cavities; pleuritic exudations, and even gangrene.

The first thing noticed when the abdomen was opened was an unusual pallor of its contents. The colon was over-distended with gas, and contained only a slight amount of soft fæcal matter. The lower portion of the ileum, and several coils of the small intestine were bound together and adherent to the lower border of the pelvic cavity on the right side by firm and old fibrous bands. This binding down, however, had not to any marked degree occluded the lumen of the gut. Both the ileum and the jejunum were nearly empty, and at places so markedly contracted that at first it gave rise to the supposition that there was a stricture; but, on displacing what little gas remained in the lumen of the small intestine, the apparent stricture disappeared, and a similar appearance was produced at a distant point. The stomach and duodenum were distended by considerable gas. The whole alimentary tract and all the abdominal viscera, the liver excepted, were very pale.

The lesions which have been described in connection with the alimentary tract are chronic catarrh, hyperæmia, thickening and tumefaction of the mucous membrane, slaty pigmentation, hæmorrhagic erosions of the stomach, and hypertrophy and muscular thickening of the stomach and the upper portion of the intestine.

The spleen was pale, soft, and larger than normal. Microscopic examination failed to show anything abnormal. It weighed 8 ounces (226.796 grams).

Little or no mention is made of the spleen in histories of autopsies in diabetic cases, but Andral speaks of a singular induration of this organ, its parenchyma being so dried up that not a drop of liquid followed incision and pressure.

The sexual organs were not specially examined, as there was no gross change which attracted attention.

The change which has been recorded is atrophy of the testicle in some of the younger subjects.

Both kidneys were very much enlarged. The left one weighed 10½ ounces (297.670 grams); the right, 10 ounces (283.495 grams). Their capsules were normal in thickness and non-adherent, excepting at one or two points where a large vessel connected the capsule with the underlying parenchyma. The renal surface. after enucleation of the kidney from its capsule, was perfectly smooth. Both the free and cut surfaces were very pale, and the latter looked quite granular to the unaided eye. The cortex was very much thickened, being about four times as deep as in a normal organ. The markings of the cortical arches were distinct and straight, and, by their deep color, gave evidence of apparent congestion. No cysts were found.

The microscopic examination gave no evidence of a diffuse lesion, but all those which are so common to a chronic parenchymatous metamorphosis of the kidneys were present. The lesion was found to be located in the epithelial cells of the uriniferous tubules, and in the walls of the smaller arteries and vessels entering the Malpighian tufts. The epithelial corpuscles in every portion of the organ were in a state of advanced and extensive granular metamorphosis, each individual cell being enormously enlarged, and in most instances all evidence of a nucleus obliterated.

The destructive process in this instance differs from the ordinary parenchymatous metamorphosis, and has been described as a necrosis of the epithelial elements. Regarding this lesion in the light of a necrotic process, and that of ordinary parenchymatous transformation in the light of a carious process, we have a good comparison for the two conditions. Fig. 44 shows the ordinary, and Fig. 45 the diabetic form.

This peculiar process caused the tubules to become larger than normal, and in some of them all evidences of a lumen had been obliterated, so that all that remained to represent the original uriniferous tubule was a space filled with necrotic epithelial cells. At other points, the basement membrane of the tubule was entirely stripped of its epithelial lining.

The intertubular tissue was rendered more apparent and thickened by an œdematous swelling which, taken together with the denuded tubules, would at first lead to the supposition that the lesion was that of chronic diffuse nephritis. (See Figs. 44 and 45.) In fact, this lesion
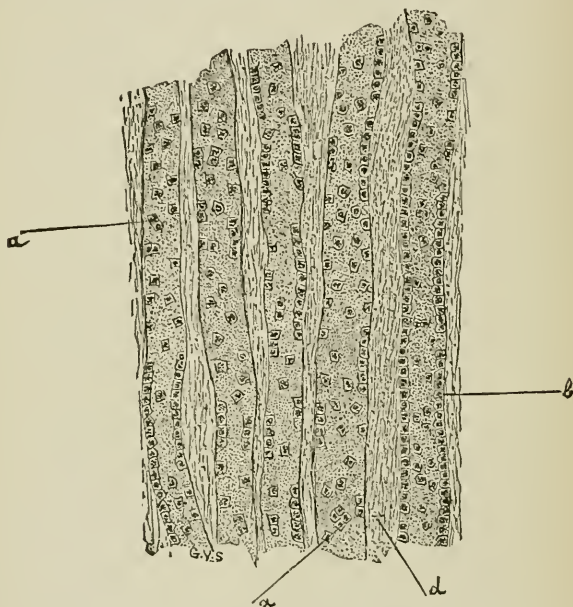
Fig. 44.—Chronic Parenchymatous Metamorphosis of the Kidney. × 350.

a, Uriniferous tubules showing the epithelial cells in a state of granular metamorphosis and desquamation; *b*, tubules showing a less marked change; *d*, œdematous intertubular tissue.

has been, and by many would be, called a diffuse nephritis. But a closer study readily shows that the intertubular tissue is free from any inflammatory exudation or recent formation in the shape of new connective-tissue and lymphoid corpuscles. The true lesion, therefore, is a metamorphotic process of the cells, brought about by an excessive amount of work; while that of the interstitial trouble is secondary, œdematous, and not inflammatory in character. None of the sections showed any granular casts in the tubules, but an occasional hyaline cast was found.

The walls of the small vessels were very much thickened by a process, the exact nature of which has not been satisfactorily ascertained, but one that may properly be called a hyaline metamorphosis. (See Fig. 46.) This hyaline metamorphosis causes a permanent thickening of the dilated arterioles, so that they ultimately become converted into non-elastic tubes opening directly into the tuft, as seen in Fig. 46, *a*.

The intimate connection between the liver and kidney, by the sympathetic system, is offered as a solution of the primary dilatation of the renal vessels, which finally become thickened and wholly unable to contract, and, consequently, remain open after death, as seen in the sections and in the drawing (Fig. 46, *a*). It was also found that
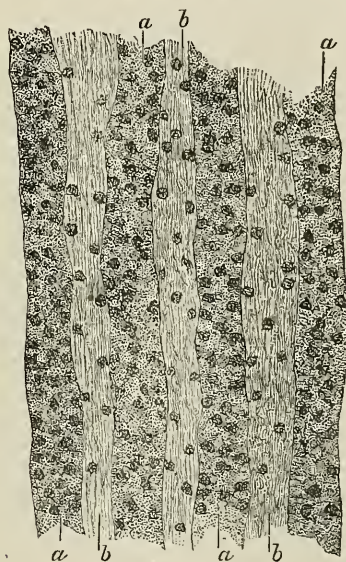
FIG. 45.—DIABETIC PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEYS, MEDULLARY PORTION, × 350.

a, Uriniferous tubules distended and occluded with necrotic epithelium; *b*, swollen œdematous, and non-inflammatory intertubular tissue, with an occasional epithelial cell.

the lumen was of more than twice the normal size, and that this condition extended up to and even through the capsule of Bowman, until the coil of vessels was reached. This lesion was not so advanced in every vessel, but all of them were more or less involved.

This enormous thickening and loss of contractility easily explains the abundant flow of urine. The pressure exerted upon the tuft of vessels within the Malpighian capsule, or upon the dilated or expanded extremity of the uriniferous tubule, is governed by the con-

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tractility of the arteriole just anterior to it. If, for any reason, this is constantly dilated, and its walls are thickened, it loses its normal contractility, and a great volume of blood is constantly poured into the tuft of vessels. This, with the unequal strain upon these vessels, from the constantly varying blood-pressure, weakens their walls and permits of a more abundant escape of water from the blood, and, consequently, a more copious volume of urine. This view is substantiated by pathological and clinical data, for there are three other lesions of the kidneys in which this or a similar transformation of the vessels is met with; and in every instance the lumen is increased and the walls are thickened, a copious discharge of urine being the in-
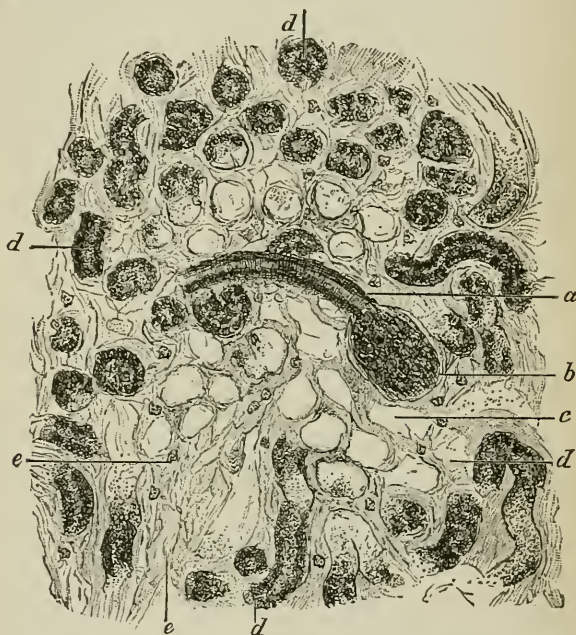
FIG. 46.—DIABETIC PARENCHYMATOUS METAMORPHOSIS OF THE KIDNEYS, CORTICAL PORTION, × 350.

a, Hyaline transformation of an afferent vessel; b, a Malpighian tuft; c, basement tubes stripped of their epithelium; d, tubules filled with necrotic epithelium; e, œdematous inter-tubular tissue.

variable rule. The three conditions referred to are the well-known cirrhotic or red atrophy of the kidneys, the waxy kidneys, and one form of chronic diffuse nephritis.

The capillaries of the glomeruli had a peculiar waxy and trans-lucent appearance, but did not respond to the ordinary test for amy-loid material.

The nuclei of the cells covering the vessels of the tuft were very

indistinct and often imperceptible. The capsule of Müller was also the seat of the same œdematous thickening as was noted in the intertubular tissue. There was an absence of blood in the kidneys, which may have accounted for the suppression of urine which existed before death.

In the second case, the renal lesion was identically the same as in the first. In the third, the lesion was practically the same, but the destruction of the epithelial corpuscles was more marked, many of the tubules being entirely stripped of their epithelial coating. The epithelial cells in situ and the vascular changes were the same in all three.

In all, the kidneys ranged in weight between 8 and 11 ounces (226.796 and 311.844 grams).

In the majority of the recorded necropsies, a lesion of the kidneys has been noted, apparently from gross appearances. The organs are spoken of as being enlarged, hyperæmic, and with a hypertrophic swelling of the epithelium. The more recent writers speak of the change in the cells as a necrotic transformation, similar to that already described.

The hilum of the kidneys and the ureters presented nothing specially abnormal. The bladder was empty and contracted down to a hard ball.

Catarrh of the pelves of the kidneys and of the ureters has been spoken of as a common ocurrence. Abscesses, amyloid degeneration, and nephritic tuberculosis have been described as being found after death.

The liver was considerably enlarged and dark in color, contrasting strongly with the pallor of all the other viscera. Its weight was 90 ounces (2,551.458 grams). It was tested for amyloid transformation, but none was detected. When cut into, it offered rather more resistance than is usually the case in a normal organ. No further macroscopic evidence of cirrhosis could be detected. The external surface was perfectly smooth, with a few spots of chronic perihepatitis. Throughout the entire cut surface, there were found numerous disseminated, dark-red, degenerated-looking spots or zones of hepatic tissue, which were surrounded by what appeared to be perfectly normal liver-tissue. On microscopic examination, these red zones were found to be composed of hepatic cells in various stages of retrograde metamorphosis. In some instances, the nuclei, the protoplasm, and even the outlines of the corpuscles were obliterated by the granular metamorphosis and swelling of the epithelial cells. The central portion of these zones showed the most marked degenerative changes. The destructive metamorphosis grew less and less marked as the periphery was approached, and finally blended

with the surrounding liver tissue, in which the hepatic cells were found to be perfectly normal. None of the epithelial corpuscles showed the fatty degeneration, with the formation of fat droplets, so common in the acute and disseminated hepatic metamorphoses of acute blood diseases. The intervening normal hepatic tissue will account for the long duration of the lesion and the reason for improvement under proper treatment. The duration of the disease may have depended, therefore, upon the rapidity of the hepatic metamorphosis. On account of the difficulty of localizing a central vessel with certainty, it was impossible to determine positively at just what point of the circulation the centres of these degenerated foci were located.

Another interesting lesion was a marked dilatation of the hepatic capillaries, with a thickening of their walls and the development of a slight amount of interstitial tissue.

The peculiarity of this interstitial new formation was that it surrounded each individual cell, or a cluster of two or three, and ran along the walls of the intralobular plexuses, instead of the walls of the interlobular vessels, as is commonly the case in ordinary cirrhosis. In this respect, the lesion bore a very strong resemblance to, if it was not, a true syphilitic sclerosis of the liver.

This general formation of new tissue undoubtedly accounted for the resistance to the knife so noticeable when the organ was first cut.

Fig. 47 very accurately represents the changes in the liver, as seen under the microscope. The same can be said of those showing the appearances in the lungs and kidneys.

The thickening of the walls of the hepatic capillaries, already alluded to, was due to a hyaline transformation similar to that found in the renal vessels.

In the second case, the hepatic lesion was similar to, but more extensive than that of the first. There was not a single epithelial corpuscle found in any of the sections that did not show this marked metamorphotic change, the protoplasm being packed by minute granular and fatty particles. Here and there a cell was found with a large fat droplet or globule similar to the condition found in fatty infiltration. There was also a marked congestion of the intralobular capillaries, many of them being distinctly distended with red blood-cells. There was also a marked intralobular sclerosis and thickening of the walls of the portal capillaries. The liver was decidedly enlarged.

In the third case, the patient had been a heavy drinker prior to his glycosuria. In his case there was marked interlobular sclerosis, but aside from this, the lesion of the liver was the same. There was

the marked parenchymatous metamorphosis of the hepatic cells, also the marked intralobular sclerosis and thickening of the portal capillaries.

There was a very striking similarity in the change in the hepatic cells, and, in each, the intralobular sclerosis, with thickening and dilatation of the intralobular capillaries, was a decided lesion. There was some congestion in all, but it was particularly marked in the
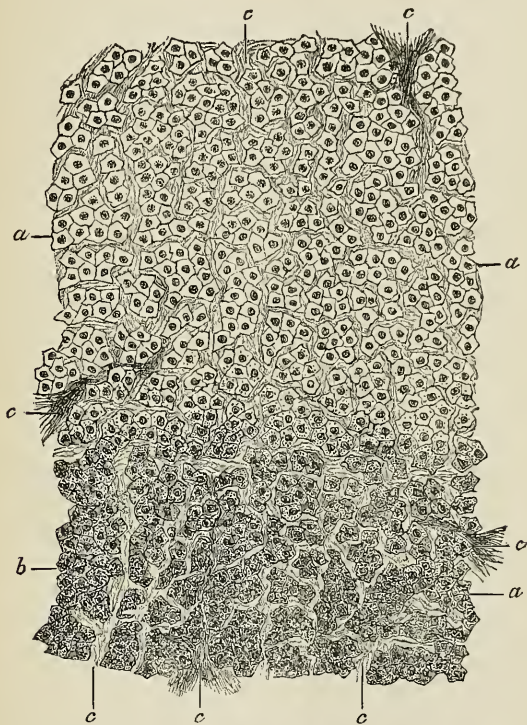
FIG. 47.—DIABETIC METAMORPHOSIS OF THE LIVER.

aa, A zone showing normal hepatic cells; *ba*, a zone showing parenchymatous metamorphosis of the hepatic cells; *c*, portal systems and intralobular cirrhosis.

second case. The weight of the liver in the last case was ninety-four ounces (2,644.856 grams).

Finding such a close correspondence in the changes in the hepatic and renal epithelial elements and in their vascular walls, has led to the firm conviction that the theory here advanced is the correct one.

Different stations of life were represented by each, and in all there was a clear history of the imbibition of more nutritive material than

was absolutely demanded by the system. In none were there any nerve symptoms or lesions.

The descriptions which have been given of the changes occurring in the liver are numerous and contradictory. The major part of them appear to be based upon gross appearances instead of minute microscopic details. The various conditions which have been found are hyperæmia, hypertrophy, congestion, increase in volume from changes in the glandular cells, cirrhosis, atrophy, amyloid degeneration, the formation of abscesses, and obliteration of the portal vein. Marks of hepatic degeneration, similar to those already described, have been quite frequently met with, together with a diminution of fat in the liver, etc.

In the first case, no special change, either macroscopic or microscopic, could be made out in the pancreas. The same was true of the third case. In many of the recorded cases, however, various lesions have been found. The numerous lesions which have been recorded as found in this organ are atrophy, or atrophy with degeneration (on the other hand, it has been found small and hard), primary fatty destruction of the gland-cells, cancer, calculi, and obstruction to the duct, with cystic degeneration of the gland. In other instances, it has been found very soft and anæmic.

Including all these lesions, some form of abnormality has been detected in nearly fifty per cent of the cases. On the strength of this, some have gone so far as to locate the cause of diabetes in the pancreas.

In the first case, the only gross abnormal appearance in the nervous system was an extreme pallor of the cerebral substance. Microscopic examination of the medulla failed to reveal anything abnormal. The sections apparently represented a normal medulla, save for a little thickening of the vascular walls.

The almost innumerable experimental lesions which have been instituted for the production of glycosuria, either permanent or temporary, have not been cited; neither have the many cerebral and upper spinal lesions which have now and then been found in connection with diabetes. The reason for omitting them in detail is that they only prove one thing: that no constant or certain lesion has been shown to be pathognomonic of this disease. The majority of them sustain the theory that overloading and overworking of the liver are necessary for the establishment of a permanent diabetes. For, unless the super-nutritious condition of the portal blood, with a possible hepatic lesion, is present, the removal of the nervous injury is invariably followed by a disappearance of the glycosuria, while in the in-

curable forms of diabetes death occurs and no nervous lesion is detected, but marked lesions are found in the liver and kidneys. But, as before stated, an injury, or irritation, or undue mental depressions, may be the spark which kindles the fire, and only in this way can these numerous lesions act; for all of them are frequently met with in cases in which there has been no appearance of glucose in the urine.

In this case, the pericardial fluid, blood, and hepatic tissue were examined for glucose by Dr. Henry Rolando, house physician at the Presbyterian Hospital, who did not find it in any of the samples.

The fact that no sugar was found in the blood appears to be strong proof that the glucose does not pass out of the liver as such, but rather in the form of sugar-producing elements, the nature of which is unknown, and that the renal cells complete the formation. This hypothesis has its analogy in the formation of urea, uric acid, etc.

The practical points of interest derived from this study are, that diabetes mellitus has for its primary cause a change in the portal blood and in the hepatic tissue and vessels; that the influence of the nervous system is secondary and not primary.

Clinical History.—Glycosuria from a clinical aspect is divisible into three sets of cases: the temporary, the mild, and the severe.

The first, as the word indicates, is of short duration and soon passes away. In some incidental cases, as after pertussis, asthma, chloroform, carbon dioxide (CO_2), and other drugs, the glycosuria is almost too transient to be classed as a distinct disease. But the following is a typical example of this class. A rather obese medical student, while preparing for his examination, became suddenly straitened in his finances, and took to drinking largely of lager beer and living upon German bread. Glycosuria set in quite actively, no less than four gallons (15.924 litres) of urine being voided in twenty-four hours. Diabetic treatment was instituted, and bromides with opium administered, which caused the disease to disappear in eight weeks. Here the nervous element and supernutrition seem to go hand in hand, although the former may appear to predominate. The fact, however, that many students have the same anxiety, but do not indulge so freely in carbonaceous substances and stand the mental strain without suffering from glycosuria, tends to support the theory that there must be an increased quantity of work demanded of the liver with primary changes in the hepatic cells before the nervous system can come into play and excite the disease.

The *mild* form is occasionally met with in elderly and obese people, who have been in the habit of "living well and enjoying life," and may last for a number of years. At first they void an increased

amount of urine which contains glucose, at the same time there is some thirst, a good appetite, a little wasting, muscular weakness and mental lassitude. But upon a modified diet and appropriate therapeutic agents the symptoms all abate, and the person appears as well as ever both mentally and physically, but the urine still contains glucose, the quantity voided being nearly normal.

The *severe* form is the most common. In this the individual voids abnormally large quantities of light-yellow urine, which has a high specific gravity, and contains large amounts of grape sugar. Thirst is troublesome, the mouth is dry and parched, the tongue red or coated, and the appetite acute with a craving for carbonaceous substances. The countenance becomes pale, and the patients progressively emaciate, and are both physically and mentally weak. Upon appropriate treatment they may temporarily improve, but, as a rule, the disease is progressive, and a steady decline in all the vital forces marks its course until complications are developed and death ensues.

The symptoms of all forms of glycosuria are divisible into different sets. Those *common* to all forms are failure in strength and mental activity, with pallor of the countenance, and gradual or progressively rapid emaciation. There will be increased or unbearable thirst, with copious as well as frequent micturition. The thirst and urinary symptoms finally cause the individual to consult the physician.

The symptoms of the *digestive* tract are the increasing thirst, which soon compels the sufferer to rise at night to satisfy it. A dry red or heavily coated tongue, with an accumulation upon the lips, gums, and teeth of a saccharine substance resembling sordes. The gums are red, swollen, flabby, and recede from the teeth, which may become carious.

The salivary secretion is sometimes acid in reaction.

The sense of taste becomes more acute with a strong partiality or desire for saccharine and starchy substances. Later in the disease, it may be perverted for certain things, as for instance pepper.

The appetite and gastric digestion, as a rule, remain good or are abnormally increased, but, like the thirst, it is not satisfied even if the things most desired are taken.

As the disease advances and approaches towards the end, the digestion may become impaired. This has been attributed to the increased digestive strain, and to the limited nitrogenous diet. But from our present pathological and physiological knowledge, this loss in appetite and giving way of the digestive powers is better explained by the failure on the part of the kidneys to eliminate the effete material from the system; the alimentary tract then attempts to eliminate what the renal

organs are unable to accomplish. The digestive trouble now becomes a prominent symptom and is due to precisely the same uræmic cause so frequently witnessed in renal lesions in which the epithelial cells of the kidneys fail to effectually perform their work.

It is a well-known clinical fact, in cases closely watched, that the failure in digestion is preceded by or is associated with a diminution in the quantity of urine and sugar excreted, and a simultaneous appearance of, or increase in, albumin and casts. If the kidney lesion can be improved and more sugar eliminated with less albumin and casts, and more of the effete materials thrown off, the digestive symptoms will improve and the appetite return.

The progressive transition and interchange from a glycosuria to an albuminuria is not uncommon. In fact, many cases, if not a large proportion, show a gradual or rapid disappearance of the glucose, with a diminution in the quantity of the uric acid and the appearance of albumin and casts as the fatal issue approaches.

Diarrhœa or *constipation* may occur. The former is more frequently met with during the course of the disease. Toward the end, constipation and flatulence are developed which are uræmic in nature and often exceedingly obstinate.

Respiratory Symptoms.—The breath has been described as emitting a peculiar apple-like odor. It, like the coma, has been ascribed to acetonæmia, but it is probably of the same origin as that in connection with uræmia.

A number of pathological conditions are met with in the lungs, each one giving its special rational and physical signs. They are both lobar and lobular pneumonia, phthisis, tuberculosis, pulmonary syphilis, gangrene, hemorrhage, etc.

In one case observed, death was due to a pulmonary hemorrhage; in another, marked syphilitic changes were found; in other instances, no special change was found.

Each of the above lesions will give its special and diagnostic rational and physical signs. The pneumonococcus, the bacillus tuberculosis, or that of syphilis, may also be detected.

Circulatory symptoms are specially confined to the heart, which is often weak and intermittent, and calls for special therapeutic attention.

Nervous Symptoms.—These are muscular weaknesses and trembling, and a diminution in the sexual desire, perhaps no more than in any wasting disease. Headaches, abdominal, gastric, and wandering pains throughout the body, are not uncommon.

Diabetic Coma.—This condition, from the peculiar reaction given

to the urine by the chloride of iron, is believed to be due to the development of acetonæmia or acetone in the blood.

The opinion advanced by Dr. Satterthwaite and others, that the coma, and death which frequently ensues, is developed in precisely the same way as that of renal lesions proper, seems to be established by the more recent investigations.

The stupor or coma is insidious in its origin. There may be some prostration, headache, restlessness, and anxiety, epigastric pain, nausea, and vomiting, just what precedes any uræmic coma.

The urine is diminished in amount, and the sugar is less abundant; or total suppression is developed. The albumin and casts become more plentiful. In one instance, the quantity of urine fell from 250 ounces, 7775.874 cc., to 15 ounces, 466.552 cc. in twenty-four hours, and during the twelve hours just prior to death, there was absolute suppression; at the necropsy the bladder was empty and firmly contracted. The pulse at first is high, small, and quick, but soon becomes weak, often intermits, and is absent at the wrist; the temperature at first is a little elevated, but it soon falls to normal or below. The breathing is rapid, labored, and superficial. In some instances, the mind is disturbed and delirium precedes the coma.

A decrease in the quantity of urine and sugar, and an increase in albumin and casts, should always be looked upon with anxiety, and a fatal coma suspected in the near future.

Ocular Symptoms.—A number of lesions have been narrated in connection with this disease. Diabetic cataract, with a loss of vision, is perhaps as frequently mentioned as any.

But all the lesions that occur in any form of chronic renal disease may be met with, viz., retinal thrombosis, embolism, hemorrhage, or atrophy, fatty embolisms of the retinæ, and the various forms of retinitis and neuro-retinitis. With these, there will be specks before the eyes, dimness of vision, or blindness. An ophthalmoscopic examination only can decide the nature of the lesion.

The acuteness of hearing is, in some instances, diminished, but more often tinnitus aurium is a troublesome symptom.

It appears from clinical observation that sugar, like urea, is occasionally eliminated by all the excretory glands, and hence the finding of glucose in the perspiration, tears, and other excretions and secretions is explained. This, however, does not seem to be of frequent occurrence, and is somewhat doubtful.

Integumental Lesions and Symptoms.—Extreme dryness of the skin is among the early symptoms. With the complicating lesions of the

lungs, hectic sweats may become marked; unilateral sweating has been noted in a few cases.

Itching of the skin, sometimes extending over the greater part of the body. But this symptom is usually most marked in females and is limited to the genital regions, and appears to be excited by the frequent micturition and accumulation of the saccharine particles among the hairs of the parts. The meatus urinarius in males becomes irritated and inflamed. An eczematous erythema is occasionally developed. Pruritus vulvæ also occurs in some cases. Late in the disease, furuncles and even carbuncles are developed, and the latter may act as a potent cause in producing a fatal issue.

Spontaneous thrombosis and *consecutive gangrene* of the extremities or other parts is also met with in five to six per cent of the cases. If the lungs are included, it is much more frequent. Any slight injury may be sufficient to excite a destructive inflammation.

Falling out of the *nails* has once been observed.

Œdema of the extremities may be developed, but this is rarely seen, for, like all conditions when large quantities of water are constantly expelled from the body, it is not likely that much will transude from the blood-vessels and accumulate in the perivascular spaces.

Urinary Symptoms.—The quantity is abnormally large, sometimes reaching as high as six or seven hundred ounces (18,662.097 c.c. or 21,772.447 c.c.). It is usually transparent, but has a heavy appearance and is acid in reaction. At first there is no sediment, but when vesical catarrh is excited, or much uric acid is excreted, a more marked deposit will be found. The color is pale yellow, and its odor has been compared, when fresh, to a faint whey-like fragrance, but when fermenting to that of sour milk. The specific gravity is abnormally high, ranging from 1.030 to 1.060, the usual range being from 1.020 to 1.030. In this respect it differs from all the other conditions in which there is an abnormally large quantity of urine voided. Sugar, however, may be found in urine having a specific gavity as low as 1.008 and perhaps lower, but this is exceptional.

The urea is increased in quantity, which would naturally be expected, from the unusually large amount of nitrogenous elements ingested. The uric acid is also increased for the same reason, the quantity of the latter often being so large that it is spontaneously precipitated in the crystalline form.

Albumin is rarely found early, but as the disease advances and the metamorphotic changes in the kidneys become more marked, it often makes its appearance. In all the cases under observation, this was found to be true, and if every sample was examined for albumin, a

large proportion of cases, if not all, would be found to contain more
or less toward the end of the disease.

Glucose is always present at some time and generally throughout
the whole course of the malady. In occasional cases, sugar may be
absent for a time and the urine may be heavily loaded with uric acid,
or the two may alternate. As the fatal end is approached, the
amount of sugar declines, while the amount of albumin steadily
increases. A partial or complete interchange between the glucose
and albumin may occasionally be witnessed.

On account of the constant danger from the renal lesion, the urine
of every diabetic subject should be carefully analyzed at least once a
week. By so doing the physician is best prepared to meet and ward
off the approaching danger, and to combat it when it does come.

There is no microscopic object typical of the diabetic state, but
when the renal lesion is fully established casts are found. After the
urine has stood and fermented, the finding of the thali of the saccha-
romyces cerevisiæ renders the presence of sugar positive.

A number of other substances have been described as occurring
in the urine, viz., hippuric acid, acetone, inosite, cholesterin, alcohol,
oxalate of lime crystals, etc. But up to the present time, no
really practical inference has been drawn from them.

Diagnosis.—This rests exclusively upon finding glucose in the urine.
The general history in a large proportion of the cases is characteristic.
If the urine of every new case be tested for the presence of sugar and
albumin independent of its specific gravity, as should be the universal
rule, no case will pass undetected. In those instances where the
interchange occurs between the sugar and uric acid, an error might
occur if only one examination was made, but repeated trials usually
reveal its presence.

Prognosis.—In the *first* or temporary form, it is good. In the
second class or mild variety, it is also good, the patient living for a
number of years, five, six, or seven, or even more. With the *third* or
severe type, the prognosis is always unfavorable. They may die within
a few hours or not for several years after the detection of the glyco-
suria.

When the disease apparently lasts but a few hours, some questions
may justly be entertained as to the actual duration. In the majority,
the average course is from one to two years after pronounced symptoms
have developed.

Treatment.—This is a disease which taxes the physician's skill as a
therapeutist to its utmost capacity. Having accepted the above
theory of diabetes, it plainly shows that no one drug or remedy can

be expected to combat the numerous physiological problems. No one medicinal agent can be expected to diminish the supernutrition, renal and hepatic metamorphosis, nervous irritation, and circulatory abnormalities. The disease calls for a wide therapeutic range to combat it successfully.

The excess of nutriment sent to the liver must be cut off or so regulated that it will cause the least possible strain on an already weakened hepatic digestion. In this way nutrition may be improved, and the liver cells given a chance to recuperate their wasting powers.

To cut off all starchy and sugary substances at once is often too great a change to the system and makes the patient absolutely worse; sometimes exciting an albuminuria with alarming uræmic symptoms. Many cases will do better to cut off the carbonaceous articles of diet one by one, at the same time gradually increasing the nitrogenous. Others appear to do equally well on a limited amount of the mixed diet. It will require no little skill to decide this question wisely.

The nervous system must not be neglected, as it plays no small part in all the digestive processes, and especially in influencing the hepatic functions. It must be stimulated or depressed, as each individual case may seem to require, until its influence upon the functions of the liver is brought as nearly to the normal as possible.

In many instances, there appears to be an over-excitability of the nerves, which the bromides are just sufficient to regulate; in others, opium and its alkaloids have to be employed; codeia perhaps holding the first place among the remedial agents. This action of opium and its alkaloids is not simply upon the nervous system, but is almost as complex as the disease itself. It acts as a sedative, not by its depressing influence, but by its stimulating properties upon the nervous centres, and upon the circulation by stimulating the heart and producing an even tension of the blood pressure, and also by retarding oxidation.

The vascular system also requires especial attention on account of the changes in the vessels of the liver and the renal arterioles. All remedies which regulate the heart's action and cause its movements to remain steady will have a tendency to institute improvement. The vascular tension should be kept as nearly even as possible, for, by so doing, the hepatic congestion will be least marked, nutrition will be most perfectly effected, and secretion and excretion will be raised to the necessary standard. For this, ergot or ergotine may be said to hold the first place. Stimulating as they do the vaso-motor system,

and causing a steady contraction of the smaller arterial vessels, the general circulation becomes more even.

By these combined remedies the nervous system works evenly, the heart strongly, and the circulatory pressure is steady, and, as a result, the hepatic circulation is rendered more uniform, its work is more perfectly performed, and less strain is brought to bear upon the renal cells and the Malpighian tufts. The effete materials are more completely removed and nutrition is raised to the highest possible degree, which gives Nature a chance to repair the primary hepatic damage, and, consequently, all the secondary changes are benefited or removed.

If the disease be fully appreciated in all its complex physiological changes and abnormalities, its early recognition with appropriate treatment suggests the possibility of a cure; this is indicated from the rapid recovery in the temporary variety and the long-continued improvement in the mild form. The temporary case already cited, page 183, would have become a confirmed diabetic had he continued the excessive use of the carbonaceous substances.

Early recognition, therefore, is absolutely essential, and especial attention should be paid to the relief of the kidneys, for the sugar-forming elements are picked up from the blood and thrown into the uriniferous tubules by the action of the renal cells, causing them, first, to hypertrophy, and then to undergo retrograde changes, until finally there is developed a true metamorphotic lesion with albumin or casts and uræmic symptoms to prove its presence. It, therefore, appears that in the epithelial corpuscles of the uriniferous tubules lies the turning point of the disease in a large measure. So long as we can protect and preserve the renal epithelial cells, just so much longer can the life of the individual be prolonged. But when they once begin to fail, and albumin or casts appear in the urine, the duration of life is placed in jeopardy. If syphilis has anything to do with exciting or keeping in motion this fatal disease (not an improbable supposition), the anti-syphilitic treatment should be instituted and persisted in.

The general principles only of the diet treatment have been dealt with in this chapter, as the minutiæ must be regulated to the requirements of each case.

The diet table of Professor Austin Flint, Jr., is appended. From this elaborate list any one can adjust the demands of individual cases.

Breakfast.

Oysters stewed, without milk or flour; clams stewed, also without milk or flour; beefsteak, beefsteak with fried onions, broiled chicken, mutton or lamb chops; kidneys, broiled, stewed, or devilled; tripe, pig's feet, game, ham, bacon, devilled turkey or chicken, sausage, corn beef hash without potatoes, minced beef, turkey, chicken, or game, with poached eggs. All kinds of fish, fish roe, fish balls, without potatoes or flour; eggs cooked in any way except with flour and sugar; scrambled eggs with chipped smoked beef; picked salt codfish with eggs; omelets plain or with ham; smoked beef; kidneys; asparagus points, fine herbs, parsley, truffles, or mushrooms.

Radishes, cucumbers, water-cresses, butter, pot-cheese.

Tea or coffee with a little cream, but no sugar. (Glycerin may be used instead of sugar, if desired.)

Rolls, pancakes, fritters, griddle cakes, etc., made of gluten bread only and eaten with butter, no syrups or sugar.

Light red wines for those who are in the habit of taking wine for breakfast.

Lunch.

Oysters or clams cooked in any way, except with flour or milk; chicken, lobster, or any kind of salad except potato; fish of all kinds; chops, steaks, ham, tongue, eggs, crabs, or any kinds of meat; head-cheese.

Red wines, dry sherry, or Bass' ale.

Dinner.

Raw oysters, raw clams; consommé of beef, of veal, of chicken, or of turtle; consommé with asparagus points; consommé with okra, oxtail, turtle, terrapin, oyster or clam, all without flour or milk; chowder, without milk or potatoes ; mock turtle, mullagatawny, tomato, gumbo fillet.

Fish.

All kinds of fish, lobster, oysters, clams, terrapins, shrimps, craw fish, hard-shell crabs, soft-shell crabs. No sauces containing flour, unless gluten flour be used.

Relishes.

Pickles, radishes, celery, sardines, anchovies, olives.

Meats.

All kinds of meats cooked in any way, except with flour; all kinds of poultry without dressings. containing bread or flour; calves' head, kidney, sweet breads, lamb fries, ham, tongue; all kinds of game; veal, fowl, sweet breads, etc., with currie, but not thickened with flour, and no liver.

Vegetables.

Truffles, lettuce, romaine, chickory, endives. cucumbers, spinach, sorrel, beet tops, cauliflower, cabbage, Brussels sprouts, dandelions, tomatoes, radishes, oyster plant, celery, onions, string beans, water cresses, asparagus, artichokes, Jerusalem artichokes, parsley, mushrooms, all kinds of herbs.

Substitutes for Sweets.

Peaches preserved in brandy without sugar; wine jelly without sugar; gelée au kirsch without sugar; gelée au rhum without sugar; omelette à la vanille without sugar.

Miscellaneous.

Butter, cheese of all kinds; eggs cooked in all ways except with flour and sugar; sauce without flour or sugar, and thickened if desired with gluten flour; almonds, hazelnuts, walnuts, cocoanuts; tea or coffee with a little cream, and without sugar. (Glycerin may be used instead of sugar, if desired.)

Bread made with gluten flour.

Alcoholic Beverages.

Clarets, Burgundy, dry sherry, Bass' ale, or bitter beer. No sweet wines or malt liquors.

Prohibited.

Ordinary bread, cake, etc., made with flour and sugar; desserts made with flour and sugar; vegetables, except those mentioned above; sweet fruits.

Gluten flour and diabetic bread may be obtained in New York from the Health Food Co., 74 Fourth avenue. This bread and flour should be used moderately, as it is not entirely free from starch and sugar-producing elements.

The diet list of Professor Andrew H. Smith is also given· This is

not strictly speaking a diabetic table, but one so arranged that, by striking out certain articles of food or drink, it can be utilized in regulating the diet of patients suffering from renal or hepatic diseases as well as diabetes.

Diet List.

PATIENT MAY EAT.

1. Oysters or Little Neck clams in season, in any form, except when fried or served with sauces of hot butter, flour, etc.

2. Soups. Broths of ordinary meats, poultry, and game; soups not thickened or mealy, and not containing any vegetables, save those mentioned in this diet list.

3. Bread. Stale or toasted; rye bread.

4. Fish of all kinds, with certain exceptions. No fried fish should be eaten.

5. Meats. Lean mutton, beef, lamb, veal, tongue, and sweet breads.

6. Poultry and game of all kinds, except duck and goose.

7. Eggs and milk, with or without cream.

8. Vegetables. Greens, spinach, lettuce, water-cress, chickory, dandelions, French beans, Lima beans, string beans, dried beans, green peas, asparagus, Brussels sprouts, cabbage, cauliflower, cucumbers, celery, artichokes, radishes, onions, tomatoes, pickles, and olives.

9. Dessert. Jellies, flavored but not sweetened; baked apples and pears without sugar; peaches, oranges, lemons, and limes, without milk or sugar.

10. Drinks. Tea and coffee without sugar, or with very little, and with or without cream; dry wines, brandy, whiskey, only if necessary; Apollinaris, Clysmic, St. Galmier, Bethesda, Poland, Buffalo Lithia, or Bedford water.

ARTICLES OF FOOD AND DRINKS TO BE AVOIDED BY THE PATIENT.

1. Soups. Thickened, mealy or sweet, or containing vegetables specified in this list.

2. Fish. Salmon, herring, eels, sardines, and dried fish.

3. Meats. Fried meat, pork in any form; dried, preserved and potted meats; the fat of meats, meat pies.

4. Sauces. Of hot butter, or containing flour, served usually with fish, meat, or game; Mayonnaise, dressings of oil and vinegar on

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salads, the use of spices, Worcestershire, Harvey's fish sauce, Tobasco sauce, etc.

5. Butter. None, or the merest trifle.

6. Bread. No fresh or hot bread, biscuit, corn bread, griddle cakes, waffles, fritters, etc.

7. Vegetables. No saccharine or starchy vegetables, as potatoes, rice, sago, tapioca, arrow-root, corn meal, hominy, oatmeal, wheaten grits, macaroni, vermicelli, semolina, beets, carrots, parsnips, no sugar, no fried vegetables, all canned vegetables in the preparation of which sugar has been used, tomatoes, onions, and corn.

8. Cheese. None.

9. Dessert. Sweets of all kinds, custards, creams, ices, puddings, cakes, nuts, dates, and raisins, dried and candied fruit, and sweet grapes.

10. Drinks. Ales, porter, stout, beer, especially heavy beer, sweet and effervescent wines, and all alcoholic drinks, as brandies, whiskeys, gin, rum, liqueurs and cordials, except when ordered.

A well authenticated case of cure of the severe forms of diabetes has not yet been recorded, but life can be made quite endurable and prolonged for months and years. From our present knowledge, it appears that a well regulated diet offers quite as satisfactory results as the former exclusive plan. If the limited diet is to be instituted, it is far better to make a gradual and not a sudden change.

URINARY ANALYSIS.

PART II.

CHAPTER I.

URINARY ANALYSIS. INTRODUCTORY REMARKS.

The urine has long been recognized as affording valuable aid in the diagnosis of disease, and as much is being added to our knowledge in this field, it is quite important that these additions should be noted. The purpose of the following sections is to elucidate the utility and make plain the necessity of the microscope in its bearings upon practical medicine, and at the same time to simplify some of the methods in vogue.

To every one conversant with the subject, it is well known that, while much work has been done upon urinary analysis, it has been chiefly from a chemical standpoint, the clinical features not receiving the attention which they deserve. It is hoped, therefore, that these chapters may commend themselves to the readers as a contribution to clinical medicine. They are the result of much work, in the hospital, in the mortuary, and in the laboratory, which, together with several years' experience in teaching, encourages the belief that they will satisfy the long-felt need of the busy and active practitioner.

An accurate understanding of urinary analysis in its relation to clinical medicine is absolutely essential for a clear comprehension of any disease.

This statement is especially true in typhoid fever, pneumonia, scarlet fever, and in fact with *all* the acute blood diseases; and also with acute surgical conditions. In all these instances, a careful study of the urine frequently proves to be a more accurate index to the rise and fall of the diseased process than any other single symptom, enabling the physician to foretell with accuracy an approaching im-

provement or a threatened exacerbation, which is to speedily termi-
nate in a fatal issue. It places him in a position to know what to
expect, and better prepares him for coming emergencies.

Accuracy in the application of urinary analysis is not to be confined
to acute diseases and surgical conditions alone, but is largely applica-
ble in many of the chronic disorders.

The results obtained from urinary analysis and their application to
clinical symptoms, together with the effect of medicinal agents, are
unquestionably the only methods by which the mystery so long con-
nected with hepatic disorders can be made plain. In this way we
may be enabled to understand and diagnosticate hepatic diseases
almost as easily and accurately as we now do renal affections. The
recent studies which have been made in the long uncertain and mys-
terious disease, diabetes mellitus, show what can be accomplished,
and not only suggests the possibility, but strongly indicate an
approaching advance in all forms of hepatic lesions.

Chemical Composition.

The various substances which enter into the formation of the urine
have been differently stated by the numerous observers; they also
vary somewhat in reference to the relative quantities of each, but in
general there is a striking correspondence. Slight variations must be
expected, from the very fact that the examinations cannot be made
under precisely the same circumstances.

The tables of Flint and Roberts are both quite complete.

Table of Composition from Flint.

Water, ...		967.47 to 940.36
Urea (in 24 hours, 355 to 463 grains, Robin), . .		15.00 to 213.00
Urate of soda, neutral and acid, / Urate of ammonia, neutral and acid (in small quantity), Urate of potassa (trace), Urate of lime (trace), Urate of magnesia (trace).	In 24 hours, 6 to 9 grains of uric acid—Becquerel—or 9 to 14 grains of urates, estimated as neutral urate of soda.	1.00 to 1.40
Hippurate of soda, Hippurate of potassa, Hippurate of lime.	In 24 hours, about 7.5 grains of hippuric acid—Thudichum—equivalent to about 8.7 grains of hippurate of soda.	1.00 to 1.40
Lactate soda, Lactate potassa, Lactate lime.	Daily quantity not estimated.	1.50 to 1.60

Creatin,	⎰ In 24 hours, about 11.5 grains of		
Creatinine,	⎱ both—Thudichum.	1.60 to	3.00
Oxalate of lime (daily quantity not estimated), . .		trace to	1.10
Xanthin, ...		not estimated.	
Margarin, olein, and other fatty matters, · . . .		0.10 to	0.20
Chloride of sodium (in 24 hours, about 154 grains—Robin),		3.00 to	8.00
Chloride of potassium, ...		trace.	
Hydrochlorate of ammonium, ...		1.50 to	2.20

Sulphate of soda,	⎧ In 24 hours, 28 to 38 grains of		
	sulphuric acid—Thudichum.		
	About equal parts of sulphate		
Sulphate of potassa,	⎨ of soda and sulphate of potassa	3.00 to	7.00
Sulphate of lime (trace),	—Robin—equivalent to from		
	⎩ 22.5 to 37.5 grains each.		

Phosphate of soda, neutral,	⎰ Daily quantity not estimated.	2.50 to 4.30	
Phosphate of soda, acid,	⎱		
Phosphate of magnesia (in 24 hours, 7.7 to 11.8 grs.—Neubauer),		.50	1.00
Phosphate of lime, acid,	⎰ In 24 hours, 4.7 to 5.7 grains—	.20 to	1.30
Phosphate of lime, basic.	⎱ Neubauer.		
Ammonia-magnesian phosphate (daily quantity not estimated),		1.50 to	2.40

(Daily excretion of phosphoric acid, about 56 grs.—Thudichum.)

Silicic acid, ...		0.03 to	0.04
Urosarcin,		0.01 to	0.50
Mucus from the bladder, ⎰			
		1,000	1,000

Table of Composition from Roberts.

Water, ...		954.81
Solid matters, ...		45.19
		1,000.00

Urea, ...		21.57	
Uric acid, ...		.36	
Extractives. ⎰ Creatin, creatinin, ammonia, hippuric acid, xanthin, hypo-xanthin, sarcin pigments, unoxidized sulphur and phosphorus, mucus, etc., etc.		6.53	28.46

	⎧ Chlorine, ...	4.57	
	Sulphuric acid, ...	1.31	
	Phosphoric acid, ...	2.09	
Fixed salts.	⎨ Potash, ...	1.40	
	Soda, ...	7.19	
	Lime, ...	0.11	
	⎩ Magnesia, ...	0.12	
		—	16.79

BLANK FOR URINARY ANALYSIS IN FULL.

No... ..

    Date........   Name............   Address...............

Hour Voided............   Daily Quantity............

Chemical Examination.

Day and hour of examination,	Daily quantity,
Color,	Odor,
Translucency,	Reaction,
Sediment,	Specific gravity,
Albumin.	Glucose,
Proteids,	Urea,
Uric acid, etc.,	Urates,
Phosphates,	Chlorides,
Adventitious coloring matter,	Fatty matters,
Mucus,	Blood,

Microscopic Examination.

Red blood-corpuscles,	Leucocytes,
Mucus,	Uric acid,
Oxalate of lime,	
URATES,	PIGMENTS,
Amorphous,	Blood,
Ammonium,	Bile,
Soda,	Miscellaneous,
PHOSPHATES,	SPERMATOZOA,
Amorphous,	VEGETABLE ORGANISMS,
Triple,	Sphero bacteria,
Stellar,	Simple bacteria,
EPITHELIUM,	Vibriones,
Squamous,	Leptothrix,
Bladder,	Desmo-bacteria (bacillus),
Vaginal,	Fungi,
Buccal,	Penicillium glaucum,
Renal,	Torula cerevisiæ,
Ciliated,	Saccharomyces cerevisiæ,
Tailed,	

CASTS. SMALL VARIETY.	LARGE VARIETY.
Blood.............................	....
Hyaline...........................	....
Epithelial.........................	....
Nucleated.........................	....
Granular, finely...................	....
" coarsely...............	....
Fatty.....,.......................	....
Tubular...........................	....
Corkscrew....	....

Sediments of Doubtful Importance.

Lime carbonate,
Cholesterin,
Leucin,
Xanthin,
Foreign matters,
Fatty matter,
Cystin,
Tyrosin,
ANALYSIS OF CASE.

ANIMAL ORGANISMS.
    Ecchinoccocus,
    Filaria sanguinis hominis,
    Bilharzia,
    Strongylus gigas,
    Miscellaneous,

Indications as to Diagnosis and Treatment.

A condensed blank for office work is also given, and its use is strongly recommended as a great help in the study of clinical medicine.

BLANK FOR URINARY ANALYSIS.

No......
    Date........   Name............   Address........ ....
    Hour Voided............   Daily Quantity............ ....

Day and hour of examination,
Odor,
Reaction,
Albumin,
Phosphates,
Chlorides,

Color,
Translucency,
Sediment,
Glucose,
Urates,
Bile pigments,

Microscopic Examination.

Red blood-corpuscles,
Uric acid,
Oxalate of lime,
PHOSPHATES,
    Amorphous,
    Triple,
    Stellar,
EPITHELIUM,
    Bladder,
    Vaginal,
    Buccal,
    Renal,
    Ciliated,
    Tailed,
Spermatozoa,

Leucocytes,
Mucus,
URATES,
    Amorphous,
    Ammonia,
    Soda,
PIGMENTS,
    Blood,
    Bile,
    Miscellaneous,
Bacteria,
Penicillium glaucum,
Saccharomyces cerevisiæ,
Fatty matters,
Foreign matter,

CASTS,	LARGE.	SMALL.
Blood...............................	....
Hyaline...........................	....
Epithelial.........................	....
Nucleated........................	....
Granular, finely..................	....
" coarsely................	....
Fatty........	....
Tubular...	....
Corkscrew........................	....

ANALYSIS OF CASE.

Indications as to Diagnosis and Treatment.

BLANKS.

The first thing to be considered in studying the urine from a clinical standpoint is a blank upon which to record the result.

Two forms are inserted, one as a guide for further elucidation in this work, and a second as a guide in ordinary practice.

The latter only differs from the former in the omission of a number of substances of rare occurrence, and two or three of doubtful authenticity.

BLANKS should always be used, numbered, and kept for future reference, which many times will be found of great service.

The *date, name,* and *address* should be carefully noted. The hour of voiding, and the exact daily quantity, especially the latter, should be rigidly enforced.

The hour when voided. This question is one of great importance, for the reason that the normal composition varies greatly during the twenty-four hours. Therefore, unless this fact is remembered, the examiner may be misguided by the results and led into an error in diagnosis, prognosis, and treatment.

There are three ways by which this source of error may be obviated.

The most accurate method is to save the whole quantity voided during the twenty-four hours, and examine a sample of this mixed urine. But in some instances this may not be practicable, which is especially true in walking cases and in men at business. In the very warm weather of summer, it may not be wise to save the urine for the whole twenty-four hours, on account of the changes resulting from fermentation.

Under such circumstances, a very fair average sample can be obtained by instructing the patient to collect that passed at night before retiring and that during the night, if any, and that voided in the morning upon rising. Great care should be exercised in having all

receptacles perfectly clean, as patients are apt to think moderately clean vessels sufficiently good to collect urine.

The only difference now as compared with the total daily quantity is a larger quantity of the solids, and consequently such a sample will be of higher specific gravity, by two or three or more degrees. This is specially true in larger cities, where the heaviest meal is taken late in the day.

By taking that passed upon rising, a little lower specific gravity will be obtained, and one which approaches more nearly to the daily average.

By one or both of these methods very nearly accurate results will be obtained, and any gross error be avoided.

In all important cases, the exact quantity discharged during the twenty-four hours must be collected and accurately measured. This should be insisted upon as *absolutely indispensable*.

If only one of the daily passings is to be examined, the hour of voiding should be noted, and then by remembering the daily variations, error may be avoided.

In studying renal diseases, it is always well to note the number of times the individual is compelled to empty the bladder.

FIG. 48 —GLASS CYLINDER GRADUATED EITHER IN OUNCES OR CUBIC CENTIMETRES.

The kind of receptacle for collecting the total daily quantity is of no practical importance, so long as the exact quantity is accurately determined, and the receptacle is kept closed. Long graduated cylinders, with or without stoppers, have been recommended; the latter are preferable. Graduated bottles answer very well, or it may be collected in a number of smaller receptacles, and then mixed and measured.

CHAPTER II.

CHEMICAL EXAMINATION.

Having ascertained those facts which must be obtained from the patient or nurse, the next step is to institute a thorough chemical analysis, and then set aside a sample in a conical glass for the microscopic examination. The reason for using a conical receptacle is, that in many instances, when a microscopic examination is most essential, the urine contains but little sediment, and unless it is collected in this way, very valuable information is easily overlooked.

FIG. 49.—CONICAL RE-
CEPTACLE for collecting
sediment (Witthaus).

Day and hour of examination.—It is of great importance to note accurately not only the day, but the hour of examination of each sample tested. In this way the number of hours that have elapsed since the urine was passed can easily be computed.

The reason for laying so much stress upon this point is, the rapidity with which urine undergoes decomposition, and the numerous new products developed by its fermentation. By remembering this, due allowance can be made, when the source of error cannot be otherwise obviated. A calculation, however, should never be allowed to take the place of a fresh sample and an early examination if it can possibly be avoided.

For absolute and indisputable accuracy, all urine should be analyzed within twelve hours after its discharge from the bladder.

In case this is absolutely impossible, it may be filtered, for in this way some of the mucus is removed, and for a time, at least, fermentation is retarded. Filtration will, of course, hold back casts and any solid matter, and for this reason, in the majority of cases, it is impracticable.

The presence or absence of the mucus appears to influence to a considerable degree the rapidity with which fermentation is established. If the mucus could be dispensed with, without losing other important ingredients, it would be of great aid in many instances.

When the urine is first expelled, it contains no free acid; its acidity

at this time being ascribed to the biphosphate of soda. If then, as soon as the urine is voided, we add a few grains of salicylic acid, chloral hydrate, or some mild disinfecting agent, fermentation may be delayed for days or hours. This is essential when the urine is to be sent any distance for examination. By observing these rules, the most accurate results will be obtained.

If casts are to be specially sought for, the patient should be instructed to collect separately the urine voided three or four hours after the heaviest meal of the day, provided, of course, that there is a fair quantity of urine discharged at that time.

A still more certain way for securing casts is to place the patient upon hydragogue diuretics, with copious draughts of water, and have the urine collected as soon as free diuresis is established. In this way large quantities of casts are dislodged, and are found in abundance. After a discharge of casts, lasting two or three days, the urine will often be found free from them, and it may remain so for several days. It not unfrequently happens, in some forms of renal lesions, that this alternation between an abundance and scarcity or absence of casts becomes one of the characteristic symptoms of the disease.

DAILY QUANTITY.

The normal quantity of urine expelled from the bladder during the twenty-four hours has been variously estimated by different observers. A good general average is from forty to fifty ounces. This will be assumed as the normal standard for further comparison.

A temporary variation of ten, fifteen, or even twenty-five ounces either way, does not in itself indicate an abnormal condition of the kidneys, but if prolonged, it is a deviation from the normal standard, but does not of necessity indicate disease. The differences in the solidity of the food, the quantity of fluid taken, the activity of the skin and alimentary tract, and the surrounding temperature will often explain the change.

If, however, all these conditions remain about the same from day to day, and are then associated with a persistent increase or decrease in the total quantity voided, a careful and complete examination should at once be made. This positive change in quantity is frequently the first symptom to attract the attention of the patient and cause him to seek medical advice.

A continued increase is indicative of chronic interstitial nephritis; one form of chronic diffuse nephritis, in which there is a hyaline metamorphosis and permanent dilatation of the afferent vessels of the glomeruli; amyloid or waxy kidneys in which a similar condition

of the afferent vessels is present; polyuria, diabetes insipidus, or diabetes mellitus.

A continued decrease is indicative of a lesion of the kidneys involving the epithelial cells, and occurs in acute and chronic parenchymatous metamorphosis of the kidneys; also in chronic congestion there is a persistent diminution in quantity.

A close study of the clinical history, and a careful chemical analysis and microscopic examination of the urine will enable the examiner to readily and accurately decide which of the above diseases is the cause of the persistent increase or decrease in the urine voided daily.

In some forms of the chronic diffuse nephritis, there may be a continued decrease for several days, and then the quantity will increase again. This fluctuation is often repeated, and consequently becomes a diagnostic element in itself.

The relation existing between quantity and specific gravity is one of the most important facts in connection with urinary analysis. It will be fully considered when studying the specific gravity.

It is almost impossible to determine with absolute certainty the quantity voided by a female, for the reason that some will unavoidably be lost when at stool. In case there is no movement of the bowels, not an uncommon occurrence, the exact quantity can be determined.

COLOR.

It is almost impossible to determine with accuracy the varying shades of color which may be met with in urine. For this reason the four general headings, adopted by other writers upon urinary analysis, will be retained, as they can be readily appreciated and recognized by all; viz., *pale, normal, golden* or *orange-yellow, high-colored*, and *dark urine*. In speaking of color, it should be applied to a considerable quantity or to its appearance when in the chamber. Viewed in a bottle or test-tube by transmitted light, it will be much lighter than in the first receptacle. For this reason, what may appear to be dark urine to the patient will be considered much lighter in color by the examiner, and give rise to a variance of opinion. This should be remembered in taking the patient's statements in regard to color.

(*a*) *Pale urine* varies from a clear liquid closely resembling pure water to a light straw-yellow color, or to the normal, and is usually abnormal.

(*b*) *Normal colored* urine ranges anywhere between a rich golden yellow and a deep orange-yellow.

(*c*) *High-colored urine* ranges between a reddish-yellow and a decided red.

(*d*) *Dark urine* ranges from a reddish-brown to a blackish or deep black.

Pale urine is due to an increase in the watery constituents resulting either from copious draughts of water or liquids, a rapid excretion, or to a diminished perspiration following exposure to cold. A variation in the quantity of pigments excreted will also vary the color.

A thickening of the walls of the vessels, and especially of the arterioles of the kidneys, by diminishing their power of contractility, always increases the quantity of water discharged from the body. These vessels, and especially the afferent to the glomeruli, having lost their power of contracting and expanding with the constantly varying blood pressure, are no longer able to regulate the pressure in the capillary tuft of the glomeruli and, as a result, the now increased hydrostatic pressure brought to bear upon the tufts over-distends their capillaries, weakens their walls, and forces the water of the blood into the uriniferous tubules more rapidly, thus greatly augmenting the flow of urine.

This fact is well borne out in the amyloid degeneration of the kidneys, in the sclerotic kidneys, and in that variety of chronic diffuse nephritis where there is a hyaline transformation, with thickening and dilatation of the afferent vascular walls. In all of these three conditions, this change in the vessels is a noticeable feature of the lesions, and in all an abnormally large quantity of urine is one of the pronounced symptoms.

On the other hand, in all forms of renal disease in which the vessels are not thickened and dilated, but retain their contractility, it is a noticeable fact that the quantity of urine excreted is, as a rule, below normal.

In every instance where an opportunity has presented for making a necropsy in diabetic subjects, a careful study of the renal organs showed a marked thickening and dilatation of the afferent vessels of the glomeruli, which easily explained the large flow of urine in this disease. This inability on the part of the system to regulate the discharge of water is undoubtedly the true explanation for the extreme thirst.

The quantity of urine is also increased in anæmia, diabetes insipidus, after hysterical fits, asthmatic attacks, and all forms of marked nervous excitement. In all of these, the urine is very pale (urina spastica), and contains little else than water. It is quite apparent that a relaxation of the vaso-motor system distributed to the splanchnic arcade is the cause which dilates the afferent vessels, increases the pressure brought to bear upon the tuft of vessels forming the glomeruli, and explains the copious discharge of urine. The urine is pale during convalescence from fevers.

Chylous urine should be classed as pale, for it lacks the yellow color of a normal sample. It is in some instances positively white, like milk, from the emulsified fat which it contains. At other times it has a muddy appearance.

High-colored urine occurs with increased perspiration, with a small daily use of liquids, with disorders of the liver in which its function is incompletely performed, and with all febrile diseases. After a hearty meal, it not infrequently happens that the urine of a perfectly healthy individual is high-colored.

In connection with the acute febrile disorders, the color of the urine often serves as a sure index to the rise and fall of the diseased process, and proves a safer guide than any other single symptom. For this reason, the urine should be carefully recorded day by day, and in some cases more frequently.

The causes of the increase in color in all acute and febrile diseases which are associated with a blood poison appear to be dependent upon the diminution in quantity and also upon the hæmatoglobinuria theory (page 107), in which there is a destruction of the red blood-corpuscles, brought about by the original poison and the increased tissue metamorphosis, setting free the blood pigment which is discharged by the kidneys. It certainly offers a reason for the high color, and accounts for the changes in the shade, with the slightest variation in the disease.

In acute yellow atrophy of the liver, and in various chronic affections of the hepatic gland, there often is an increase in the color of the urine from changes in the biliary function, and a discharge of the bile pigment or some of its derivatives. High-colored urine is not inconsistent with health, and is found after a full meal, after exercise, and in samples that have stood some time.

Dark urine is due to bile, blood, and various forms of pigments and their derivatives.

When the urine is colored by bile pigments, the shade may vary from brown to green. When colored by blood, hæmoglobin, or other pigments derived from blood, it is smoky, blood-red, coffee-colored, or even blackish.

It has been stated that a smoky tint is absolutely diagnostic of blood (Legg). This is thought to be an error, from the fact that, in connection with carbolic-acid poisoning, the same appearance is noticed. If the high-colored urine of carbolic-acid poisoning can be traced to an induced hæmoglobinuria by the acid, then the original statement is not far from correct, otherwise it is inaccurate.

Various adventitious substances also change the color of the urine.

Very strong coffee deepens the color. Large doses of rhubarb or senna will often produce a deep-yellow or reddish hue. This condition can be distinguished from urine colored by blood by the addition of a mineral acid. If the color depends upon the first cause, the urine will become brighter and of a light-yellow color; but if due to blood, it will become muddy and darker in color. Hæmatoxylon gives the urine a reddish hue; santonine in alkaline urine an orange-red, but in an acid sample a golden-yellow color. If an acid be added to such urine, it will become saffron-yellow or greenish, and resemble that containing bile pigment. Carbolic acid, creasote, and tar preparations occasionally give a blackish or even black color. With melanotic tumors, the urine often turns black upon standing or after the addition of nitric acid.

Saffron, pareira brava, beet-root, indigo, camphilia, and cochineal all tend to impart color to the urine.

All the causes of hæmoglobinuria will increase the color, viz., muscular fatigue, mental excitement, malaria, syphilis, rheumatism; malignant, septic, putrid, and typhus fevers; purpura, scurvy, phthisis; naphthol, pyrogallic acid, arseniurated hydrogen, carbon anhydride, chlorate of potash, etc.

The above appears to cover all the points which are practical in connection with the color of urine. At the same time, Vogel's standard scales of colored plates are not to be ignored, for they will often be found of service by way of comparison. Vogel divides the tints exhibited by urines into three groups, each consisting of three members: yellow, reddish, and brown or dark urines. (See plate.) The first group he subdivides into: 1st, pale-yellow; 2d, bright-yellow; 3d, yellow. The second group into: 4th, reddish-yellow; 5th, yellowish-red; 6th, red urines. The third group into: 7th, brownish-red; 8th, reddish-brown; and 9th, brownish-black urines.

There are, however, several objections which may be raised against the usefulness of Vogel's test-plates as a method by which reliable and practical information can be obtained. 1st, for those who are color-blind they are useless; 2d, unless the sample be tested in the same vessel, each time the information must be inaccurate as regards any definite quantity of pigment; 3d, no value can be placed upon the study of these colors, for the reason that any one of them may be produced by a variety of different coloring matters and circumstances; 4th, the degree of light transmitted through the fluid medium would in itself be a source of error; 5th, few are sufficiently well trained in differentiating delicate shades in color to judge accurately; 6th, it is a *noticeable* fact that the different lithographers, in reproducing the test-plates, give a dif-

ference in the shades of color. This, of course, would make no difference if the same plate was constantly used, but two persons examining the same sample and using different plates, all other things being equal, would not get the same result.

ODOR.

The odor of normal urine has been variously described, but it is a noticeable fact that it corresponds to that of the fat of the animal from which the urine comes.

When alkaline from fixed alkalies, it is said to be aromatic. Diabetic urine often has a sweetish smell, and has been said to have a whey-like fragrance when fresh, but on fermenting to have the odor of sour milk.

Urine that contains decomposing blood has a fœtid odor, while that containing bile a peculiar and often offensive smell.

The normal odor may be changed by articles of food or by drugs, viz., asparagus, onions, garlic, turnips, and by juniper berries, turpentine, asafœtida, cubebs, copaiba, oil of sandal wood, carbolic acid, alcohol, etc.

If the urine undergoes alkaline fermentation, it develops an ammoniacal odor, which often is decidedly perceptible.

It is rare that the sense of smell is of any diagnostic value.

TRANSLUCENCY.

In normal urine, when first expelled, its transparency is so nearly perfect that no appearance of turbidity is perceptible by ordinary diffused light. On account, however, of the trace of mucus obtained from the walls of the urinary tract, a faint opalescence can be detected when a sunbeam is made to pass through the sample in a lateral direction. But at the end of a few hours the mucus will subside, and appear at the lower third of the bottle or receptacle as a cloudy mass, and the supernatant fluid will now be perfectly transparent.

On cooling, if the urine be concentrated and acid, the urates will be deposited. As the sample becomes more acid, an abundant deposit of uric acid crystals may result.

Normal urine, however, under all circumstances, should at first be perfectly transparent.

REACTION.

The reaction, taking the whole quantity passed during the twenty-four hours, is, as a rule, acid. Its acidity has been ascribed by

different observers to a variety of substances, in part to free acids, such as carbonic, acetic, lactic, oxalic, uric, and hippuric. Weight of evidence, however, goes to prove that the above enumerated acids play little or no part directly in causing the reaction. It appears rather to be due to a chemico-physiological combination between the ordinary sodium phosphate of the blood and the organic acid developed in the system, by which the uric acid is united with a part of the sodium phosphate to form a sodium urate, the remaining portion being left as an acid sodium phosphate; and to this substance the urine directly owes its acidity.

From this it is readily seen that, after all, it is the uric acid indirectly which causes the reaction. This is also confirmed by the well-known fact that in herbivora, where but little uric acid is produced, the urine is normally alkaline, but when deprived of their vegetable diet, and compelled to subsist upon their own flesh, the urates and uric acid rapidly increase, and the urine becomes strongly acid.

The acidity also varies considerably during the twenty-four hours. At times, it may be neutral or even alkaline. This change in acidity was explained by Bence-Jones as an off-setting action between the acidity of the stomach and kidneys. His argument was that during digestion the acid of the blood was poured into the stomach to form the gastric juice, and consequently the urine became alkaline; but as soon as the nutritive materials were taken up by the blood, it again received this acid, and this in turn increased the acidity of the urine. In herbivora, there is no such alternation, and we know that no amount of acids administered by the mouth will change the reaction.

Roberts, in opposition to Bence-Jones, holds that the alkalinity is due to the absorption into the blood of the large quantity of nutritive material ingested at each meal. But the explanations of both Bence-Jones and Roberts fall a little short of a complete elucidation of this phenomenon. The latter theory is unquestionably more in keeping with physiological laws, but it should have gone further, for the process does not cease with the influx of the alkali; but the liver becomes occupied in receiving and transforming the newly ingested nutritive materials which are to be distributed to the various parts of the body. Consequently while this part of the work is being accomplished, the production of urea and uric acid is reduced to the minimum, and this naturally diminishes the quantity of uric-acid forming elements in the blood which can join with the sodium phosphate. As a result, the quantity of acid biphosphate formed is diminished, and this, in conjunction with the increased alkalinity of the blood, naturally tends to decrease the acidity of the urine. But as soon as this portion of the

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hepatic function is accomplished, it produces again an increasing quantity of uric acid until the next period of absorption commences. This would seem to offer a more complete explanation for the rise and fall in the acidity of the urine. It also explains the increasing acidity during the day and following the greatest amount of bodily and mental metamorphosis, and shows why, after a night's rest, the first meal is most likely to render the urine alkaline.

In some cases, the urine may remain alkaline for a whole day. It need not be considered especially, but, according to the above theory, would indicate a deficient production of uric acid; and, if the alkalinity were prolonged, would indicate a serious abnormality either due to a deficient absorption of the nutritive material from the intestinal tract, or to a deficient production of uric acid, probably the latter.

Under perfectly normal circumstances, it is true that the urine holds an inverse ratio to the amount of acid secreted by the stomach, which, by being above or below normal, will interfere with intestinal digestion, and consequently will, in a measure, alter the reaction of the urine. The acidity, therefore, decreases after food is taken, but increases as the gastric digestion advances, and is most decided at the height of intestinal digestion or after the stomach has accomplished its work.

Food and its contained elements will of necessity vary the reaction of the urine; vegetables tend to diminish the acidity, and produce positive alkalinity, while an animal diet intensifies the acidity.

After the urine has been expelled from the bladder, the acidity for a time increases, which is caused by acid decomposition. The *acid* fermentation is probably brought about by some specific ferment not yet thoroughly understood, and the development of some acid, either lactic or oxalic, or both together. As these changes take place most rapidly when exposed to air, and in urine that contains considerable mucus, the latter undoubtedly is one of the essential factors, as it has already been proved that, by filtration and removing the mucus, this fermentation is decidedly retarded.

Hofman and others, however, deny that there is any "acid fermentation;" but there certainly is often an increased acidity after the urine has been passed for a time, and this Scherer has said to be due to the mucus of the bladder.

This increased acidity often causes a precipitation of the urates and uric acid which previously were held in solution.

After a time, the acid is followed by *alkaline* fermentation. This change is brought about by the splitting up of the urea into carbonate of ammonia, probably by the influence of another ferment, which is

thought to be due to a microscopic organism which acts as a ferment, as the yeast fungus is supposed to do in producing alcohol. This alkaline decomposition does not, as a rule, occur unless the urine is exposed to air. But in some abnormal conditions it may occur within the urinary tract, either in the bladder or, less frequently, in the pelves of the kidneys.

In case the urine be alkaline when voided, alkaline fermentation soon ensues; but if strongly acid when expelled, several days will often elapse before any change can be detected.

The first product to follow the development of the carbonate of ammonia is a deposit in the sample of the earthy phosphates, which cause the urine to become cloudy, with the formation upon the surface of an opaline scum. Still later a new salt is formed by the combining of the free ammonia with the magnesium phosphate. This new salt
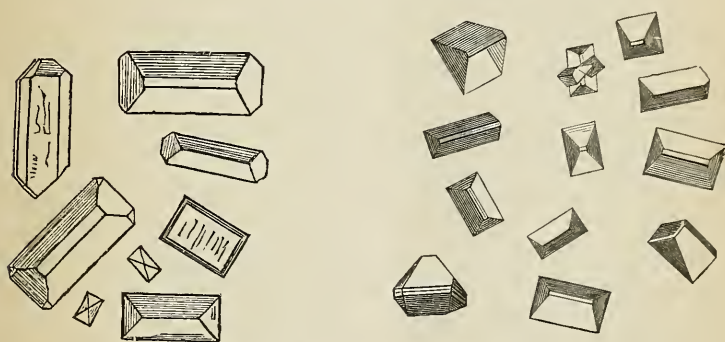
FIG. 50.—CRYSTALS OF AMMONIA-MAGNESIUM PHOSPHATE.

is known as the triple phosphate or the ammonia-magnesium phosphate.

If the urine is constantly neutral when first passed or alkaline, it indicates an abnormal condition, and calls for treatment by removal of the cause.

This constant alkalinity may be due to the fixed salts (soda and potassa) or to a volatile one, ammonia. The former are derived from the blood, the latter from the decomposition of the urea. In both instances the urine is turbid from the precipitation of the earthy phosphates.

The fixed salts can be recognized by their property to turn red litmus paper blue, which retains the color when dried; from the absence of any ammoniacal odor; and also from the presence of crystals when examined microscopically.

The ammonia also turns red litmus paper blue, but the color here does not remain after it has dried; the ammoniacal odor is pronounced, and triple phosphates are developed and found in the urine in abundance. Both these conditions occur in the bladder and upper urinary tract, and in some instances give rise to a vesical or renal calculus.

The fixed salts are said to be the least likely to give rise to this condition, as they are in an amorphous state, while the triple phosphates are supposed to favor deposition. This is, however, somewhat questionable.

These two conditions should be accurately differentiated; the former
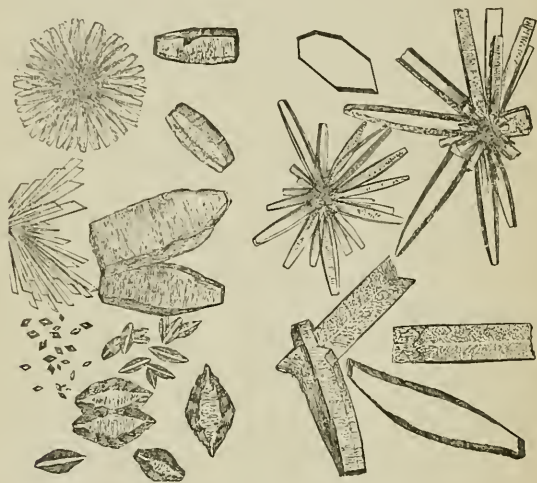
FIG. 51.—URIC ACID CRYSTALS.

is due to changes in the blood, and needs to be treated by a change in diet and internal medication; but in the latter the decomposition is primarily external to the renal cells or somewhere in the urinary tract, and the treatment is both local and systemic, but principally the former.

Abnormally acid urine is occasionally met with, and often causes a scalding sensation during the act of micturition. Outside of the body this undue acidity produces an abundant deposit of uric acid crystals, which may also be the case within the urinary tract, and it then gives rise to the condition known as gravel and the formation of renal and vesical calculi. In other cases, these uric acid crystals irritate

the mucous membrane of the bladder, in this way inducing a cystitis, which, in turn, is followed by alkaline fermentation, decomposition of the urea, and the formation of the carbonate of ammonium with the production of the earthy phosphates, which, being deposited in successive layers upon a nucleus of uric acid, ultimately forms a phosphatic calculus.

From this it will readily be seen that undue acidity of the urine when discharged from the kidneys may be followed by a discharge of alkaline urine from the bladder. This point should always be carefully considered in making a diagnosis.

In both acid and alkaline urine due to increased primary acidity, the trouble originates in a faulty action on the part of the liver, by which there is an increased production of uric acid.

This condition can be temporarily modified by giving alkalies or vegetable acids. But the most effectual and permanent treatment consists in a regulation of the diet and plenty of open-air exercise. Carbolic acid in one-minim doses, in water, three times a day, in some instances appears to prevent the formation of uric acid calculi, and relieves the symptoms of gravel.

The internal administration of fresh ox bile or the inspissated fel bovis will often do more toward improving this condition than any other form of medication. The fresh bile can be given in drachm doses in capsules before each meal, or from three to five grains of the inspissated in pill form (see page 26).

Urine occasionally is found to react both to red and blue litmus paper, and is then said to be amphoterous, but has no clinical significance.

SEDIMENT.

Normal urine, when first voided, is perfectly clear and transparent, but after standing for a few hours the lower third often becomes cloudy or opaque from the deposition of the contained mucus.

Chyle, spermatozoa, and epithelium often render the urine opaque when first voided without any further precipitation. Pus, blood, and the phosphates in concentrated and alkaline samples produce the same result. The urates in concentrated and acid solutions, as soon as cooled, produce a decided cloud, and often an abundant precipitate.

All the crystalline substances are deposited, but usually being in such small quantities they do not produce a precipitate which is perceptible to the unaided eye.

Normal urine, when voided, may be transparent and, upon standing,

become opaque. The same is true of abnormal urine. On the other hand, abnormal samples may remain perfectly clear and transparent, as for example, urine which contains glucose, albumin, or both at the same time. Both substances being perfectly soluble in the urine, it remains clear independent of its reaction. They are most perfectly soluble, however, in acid specimens.

The amount of sediment is roughly estimated by the eye.

The deposit which may form is composed of organic and inorganic substances, some being normal to this fluid, others foreign to it; each will be considered separately.

SPECIFIC GRAVITY.

This question, like that of quantity, has been variously stated. The normal specific gravity ranges between 1.017 and 1.023, and according to some writers from 1.015 to 1.025.

This variation in density, associated with the changes in the daily quantity of urine eliminated, is one of the most important points to be observed in connection with urinary analysis.

The specific gravity, as well as the quantity, will vary naturally with the amount of fluids taken and the quantity and solidity of the food.

When there is no special excess or diminution in the fluids and food taken, a close observation of the quantity and density will give the most valuable information. By the quantity and specific gravity, but especially the latter, a positive diagnosis is often to be determined.

If we have persistently a small quantity of urine with a high specific gravity, say 1.020 to 1.025 or above, it is a strong indication, in fact almost positive evidence, of parenchymatous metamorphosis of the epithelial cells of the kidneys, or a derangement in the action of the liver, which may be functional or due to some organic hepatic lesion. In such a sample, further examination will reveal the presence of albumin and casts, or an increase in the uric acid and urates, and then the diagnosis is positive.

This fact in reference to the specific gravity, so far as is known, was first advanced by Professor Satterthwaite as a strong diagnostic point in favor of parenchymatous metamorphosis of the kidneys.

A large quantity of urine and a specific gravity of 1.025 to 1.040 or 1.060 indicates the probable presence of sugar. In all cases where the quantity is above normal and the density above 1.025, sugar should be suspected and tested for. Glucose, on the other hand, may be found in urine of a low density. This, however, is the exception.

When the specific gravity fluctuates between 1.017 and 1.010 or lower, with a varying quantity of pale urine, it is strongly indicative of the existence of chronic diffuse nephritis. The finding of albumin and casts will confirm the suspicion.

With a small quantity of urine of a dark, smoky hue, and a specific gravity ranging between 1.020 and 1.012, acute diffuse nephritis is to be suspected. The finding of albumin and casts, especially blood-casts and blood-corpuscles, completes the diagnosis.

In cases where the urine is abnormally increased, and continues at sixty or one hundred ounces per day, with a specific gravity constantly ranging between 1.010 and 1.005, a sclerosis of the kidneys is indicated. If albumin and casts are absent, or seldom found, the diagnosis is almost assured.

If the quantity of urine continues very large, with a specific gravity ranging from 1.005 to 1.001 persistently, and there is a clinical history of long-continued caries, suppuration, phthisis, or syphilis, amyloid kidneys will usually be found at the necropsy. In the urine excreted by waxy kidneys pure and simple, albumin and casts are rarely present. If, however, the amyloid transformation is secondary to the other chronic forms, then albumin and casts, one or both, will be found in the urine.

Fig. 52.

C, URINOMETER with full scale, 0 to 60; D, glass for holding urine; 15, top of fluid indicating a density of 15 or 1.015.

There are a number of methods by which the specific gravity can be determined—with the picnometer, Mohr-Westphal balance, or with a hydrometer, commonly designated in connection with the urine a urinometer.

The first two are the most accurate, but least convenient. For a further elucidation of the first two, the reader is referred to works on physics.

The latter, however, deserves a word of attention, as it is the method in common use and the most practical, although not quite so accurate as the former.

The instrument should be carefully made to register densities from 1.000 to 1.060. All this can be indicated upon the stem of a single instrument, but it is much better to use large instruments, covering

only a part of this scale: one covering the space from 1.000 to 1.030, a second from 1.030 to 1.060, or better still, three, each covering twenty degrees.

The accompanying cylinder, in which they are to be used, should be sufficiently large to allow them to float easily and without adhering to the sides.

The great objection to the small urinometers with a short stem and a scale of sixty degrees is that a large proportion of them are exceedingly inaccurate, and the error has been found to be as great as thirty degrees on a single scale. It is also difficult to read them with accuracy.

Some of the small instruments having a porcelain stem with the scale cut upon it are quite accurate.

Pains should be taken to compare the whole scale with a urinometer of known accuracy at the different densities, and if it is then found correct, the smaller instruments may be used.

The urinometers are very convenient many times when small quantities of urine only are obtained. This difficulty, however, can be obviated by diluting the urine with equal volumes of distilled water until the larger instruments can be used. Multiply the specific gravity above one thousand by the number of volumes of water added, and then add 1,000. If three volumes are added and the specific gravity of the mixture is 1.005, multiply the five by three, and add 1,000, which will equal 1.015 as the density of the urine.

On account of the difference in density of any fluid at different temperatures, some of these instruments are furnished with a thermometer upon the float; by it the temperature can easily be determined and brought to a proper standard, and a computation made from tables constructed for that purpose.

With an instrument of this kind in which the scale of the thermometer and the urinometer have been accurately made, very close estimates can be determined.

Unless an accurate quantitative estimate is desired, this precaution is not absolutely essential, and the ordinary urinometer, which is correctly graduated, answers every purpose.

CHAPTER III.

ALBUMIN ; TESTS FOR ALBUMIN ; CLINICAL SIGNIFICANCE.

Albuminuria.—Albumin in the urine occurs under a number of different circumstances and is best divided into *adventitious,* sometimes called false, and *intrinsic,* or what has been termed true albuminuria.

The various forms of albumin found in adventitious albuminuria are hæmoglobin, and egg-albumen, a peculiar form of albumin described by Bence-Jones[1] as occurring in mollities ossium, which he designated as hydrated deutoxide of albumin (par-albumin). It is characterized by not being precipitated by heat, by nitric acid, nor by adding nitric acid to boiling urine, but if it is boiled, and then allowed to cool, a precipitate falls, and this is immediately redissolved by heating it again. A similar substance has been found in the buff coat of inflamed blood and in the albuminous fluid of pus.

Globulin or paraglobulin, acid-albumin and alkali-albuminate, peptone, hemī-albuminose of Kuhne, and fibrin should be included in the list. They all have their origin in some condition outside of the kidneys, either in an intestinal indigestion or in an incomplete hepatic metabolism.

The first or hæmoglobin is found in the urine when there has been a hæmorrhage into the urinary tract and the red blood-globules have been liquefied; or in cases of hæmoglobinuria. The presence of hæmoglobin can be ascertained by Almén's guaiac test or by Heller's potassa test. (Part II., Chapter VII.)

The globulins are precipitated by heat and by passing carbon dioxide (CO_2) through a very dilute acidulated solution for one or two hours, but this precipitate is soluble in very dilute solutions of chloride of sodium, consequently the test is quite impracticable unless this salt has first been removed or the urine diluted one or two thousand times.

The alkaline albuminates are precipitated by neutralization with

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[1] Bence-Jones, " Animal Chem.," p. 109.

acetic acid, except in the presence of the alkaline phosphates. There-
fore, if this alkalinity be overcome, they may appear, but they are not
precipitated by heat.

The acid albumins are not precipitated by heat nor by the carbon
dioxide (CO_2), but they are precipitated by neutralization, and the
presence of the alkaline phosphates does not interfere with this reac-
tion.

The peptones are not precipitated by heat, by carbon dioxide (CO_2),
nor by neutralization, but they are precipitated by alcohol in excess,
especially if absolute, and by nitric acid.

Before testing for the peptones, all other forms of albumin should
be eliminated by boiling, or better still, by dialyzation, and then the
tests for the proteids in general are applicable.

Egg-albumen is usually detected by the addition of ether, which
causes it to be precipitated, but does not affect the serum-albumin.

Adventitious albuminuria has been considered of infrequent occur-
rence, but more recent observation naturally leads to the belief that
many times the small traces of albumin detected in urine by the more
delicate tests are in reality of the adventitious variety, and do not
indicate any renal disease.

The great difficulty in obtaining valuable information from these
different albumins is the inability to distinguish one form from the
other with ease and certainty. It can, of course, be accomplished,
but it requires a very careful and often extended analysis, and conse-
quently is not, as yet, practicable. There appears to be no doubt but
that the two forms of albuminuria have been confounded, and in this
way errors in diagnosis have arisen.

In the *intrinsic* form of albuminuria, there must be some change in
the renal circulation, or in the structure of the kidneys and their ves-
sels and epithelium, for serum albumin is not, as a rule, excreted by
the kidneys while perfectly normal.

Changes in the blood, however, may produce either the adventitious
or the intrinsic albuminuria. The abstinence from salt, too free use
of eggs or egg-albumen, certain forms of indigestion during the severe
fevers, and in connection with all conditions in which the alimentary
and hepatic digestion is incompletely performed, will give rise to ad-
ventitious albuminuria. This is especially true in the latter. The
albuminates now pass into the blood and remaining unchanged or not
being completely converted into serum-albumin, they pass on to the
kidneys and are forced out with the water, causing an adventitious
albuminuria. This may in a measure explain the not infrequent oc-
currence of albumin in the urine in connection with all severe febrile

diseases in which there are no marked structural lesions of the kidneys. But more frequently the poisonous element which produces the primary disease, together with the extra work to be accomplished by the renal epithelial corpuscles, causes a decided hepatic and renal lesion to be developed, and now the albuminuria becomes both adventitious and intrinsic.

The most common cause of intrinsic albuminuria is to be found in changes in the blood, renal circulation, and structural changes in the parenchyma. It occurs in connection with congestion of the kidneys from certain forms of cardiac and pulmonary lesions, after cold bathing, and varnishing the skin.

Increased pressure in the renal arteries was at one time thought to produce intrinsic albuminuria, but later experiments are somewhat opposed to this view. But increased pressure upon the venous side is without doubt one of the great causes in producing this form of albuminuria.

Even in connection with these vascular changes, albumin does not appear in the urine until a marked metamorphotic transformation has been developed in the epithelial cells. This tends to substantiate the theory already advanced that abnormalities in the vascular pressure alone are not sufficient to cause an intrinsic albuminuria, but to this must be added metamorphotic changes in the renal epithelium and a malnutrition of the vascular walls of the Malpighian tufts. Then the albuminuria becomes intrinsic, persistent, and does not disappear until the integrity of the epithelium is restored and the nutrition of the vascular walls is raised to the normal standard.

The necessity of having retrograde changes in the renal epithelium before an intrinsic albuminuria can be developed also suggests the possibility of the discharged albumin being given off by the epithelial cells in a similar manner to the excretion of glucose in diabetes. This theory is also substantiated by the fact that the amount of albumin discharged is in direct relation to the retrograde change in the renal epithelium. If there is only a slight metamorphotic change in the epithelium, the quantity of albumin in the urine is small; but, if extensive, the amount of albumin will be large.

Cardiac and pulmonary lesions that obstruct the general venous circulation, and secondarily interfere with the free escape of blood from the kidneys, will increase the pressure in the renal veins and produce an intrinsic albuminuria. Pressure upon the inferior vena cava above the entrance of the renal veins will produce the same result. Structural lesions of the kidneys which interfere with a free escape of blood from the intertubular plexus, increase the venous pressure, and

consequently the pressure upon the capillaries of the Malpighian tuft and in this way act as a cause in producing an inherent albuminuria. This condition appears to explain the abundance of albumin in the parenchymatous group of renal lesions, the varying quantity in the diffuse form, and its absence in the truly sclerotic variety.

In all the forms of renal lesions commonly classed as Bright's, there is some change in the blood, as well as venous obstruction, and also a change in the walls of the capillaries which form the Malpighian tuft. All these changes are most marked in the parenchymatous group, least marked in the sclerotic, and intermediate in the chronic diffuse variety. In this way we have a pathological explanation for the varying quantities of albumin.

In all the forms of structural change where the epithelial cells of the tubules are primarily and principally involved, they swell and compress the interlobular capillaries and veins, and in this way increase the venous pressure, and with the blood changes, and especially those of the walls of the vessels of the tuft, produce a constant and often abundant discharge of albumin. But in structural changes in which the lesion is confined principally to the interstitial tissue with a thickening and loss of contractility on the part of the afferent vessel entering the tuft of Malpighi, there is no obstruction to the venous side, or changes in the capillaries of the tuft. Consequently there is an increased arterial pressure, with a diminished venous pressure. As a result, a greater mechanical pressure is brought to bear upon the walls of the vessels composing the Malpighian tuft, and now a constant and abundant discharge of water is the result. But the walls of the vessels seem to retain their power to a degree sufficient to hold back the albumin and consequently, as a rule, the urine does not contain albumin. It appears, therefore, that the discharge of albumin is principally due, *first*, to the integrity of the renal epithelium; *second*, to the obstruction to the circulation through the intertubular plexus of vessels, and *third* to the integrity of the walls of the vessels constituting the Malpighian tuft. In like manner it appears that the quantity of water discharged depends largely upon the condition of the afferent vessels and the intertubular plexus, principally the former. For in all instances where the intertubular plexus is free, and the walls of the afferent vessels are thickened, their lumen is expanded, and there is a loss in contractility, so that the quantity of water is invariably large.

By the above theories, based upon a large amount of clinical and pathological data, any one can easily appreciate why in some varieties

of renal lesions there is an abundance and in others an absence of albumin in the urine.

In like manner the irregularity in the quantity of urine voided can be understood, as it varies with the nutritive changes in the epithelium and the varying vascular pressure. In opposition to the changes in tension, it may be said that quantity depends upon many things besides pressure, but it appears that the other causes are only conditions which aid in determining the amount of force brought to bear upon the vessels of the Malpighian tuft, the condition of the intertubular plexus, and the afferent vessels. It makes but little difference whether this change be a direct or an indirect one; the ultimate result is the same.

Albumin may occasionally be produced by the spontaneous decomposition or liquefaction of the epithelial protoplasm of the urinary tract. This assumption is made upon the strength of an experiment performed by Prof. Satterthwaite, who removed the bladder from a necropsy subject and immersed it in a water-bath which was kept at the temperature of the body for a number of hours; the cavity of the bladder being distended with non-albuminous urine. He found that the fluid contained in the bladder rapidly became albuminous. To be sure, this is not a parallel case with the living subject, but it suggests the possibility of a similar formation of albumin in connection with retained urine and impaired nutrition of the mucous wall in contact with the fluid.

Precautions to be observed before testing for albumin.

Before applying any test for albumin, the urine should be first filtered to remove various substances which tend to make it cloudy and which would obscure the albuminous precipitate. A very ready method is to moisten a mass of absorbent cotton, wring it dry, and pack it tightly into the bottom of a *clean* glass funnel. One thing should always be remembered, and that is, to add enough urine to completely displace all the water required to moisten the cotton, otherwise only water may come through, and no reaction for albumin will occur. But if a sufficient quantity has passed through to completely displace the water, albumin, if present, will always be found.

When the urine is supposed or known to contain pus, it should first be boiled with a few drops of liquor potassæ to the half test-tube of urine (which will precipitate the albumin of the pus), and filtered. After filtration, the fluid should be faintly acidulated with nitric acid. Then the heat test, Heller's or any other test, can be employed

and the most positive information obtained in reference to the exact quantity and source of the albumin contained in a given sample.

It requires considerable pus to produce anything more than a trace of albumin, but in some cases, when only a few pus-corpuscles are found with the microscope, a large part of the albuminous precipitate may be found to be due to pus. This is due to the sample having been taken from the top of a vessel, the corpuscles having fallen to the bottom. In all cases in which a renal lesion is suspected, this question of doubt should be eliminated.

Tests for albumin.—A number of methods are in use for detecting the albumin in the urine or in solution. Some are capable of demonstrating the presence of a very minute quantity. But as yet no ready test or tests have been discovered by which an accurate diagnosis can be made between serum-albumin, egg-albumen, and many of the forms resulting from incomplete digestion and transformation of the peptones which not infrequently pass out of the body with the urine.

Many of the tests are so delicate that all the varying forms of albumin are precipitated along with the serum-albumin. Most of the albuminates are soluble at a higher temperature than serum-albumin, but the fact that the urates, oleo-resins, and some of the alkaloids are precipitated and disappear by heat when these tests are used, renders it absolutely impossible to say which substance is causing the reaction, without resorting to an eliminating analysis, which takes time and skill.

It does not appear certain that boiling eliminates all the serum-albumin; consequently, a response to some of the more delicate tests for the proteids cannot be said to eliminate serum-albumin and indicate only modified forms of the proteid substances.

The peptones, as already seen, can be detected by their precipitation with absolute alcohol, but to obtain an accurate result, the urine needs to be dialyzed. This naturally detracts from the practical value of the test, and in every instance there is a chance for an error to creep in while making the differential analysis.

Some observers are inclined to believe, and perhaps with good reason, that even the minutest trace of albumin is indicative of an approaching renal lesion which will very soon be easily recognized by other symptoms, as a confirmed and serious disease of the kidneys. Such a conclusion seems hardly warrantable, however, until we can differentiate between the adventitious and intrinsic albuminuria more readily and accurately. For it is well known that few, if any, are able to secure and maintain an absolutely perfect digestion and assimilation even under the most favorable circumstances. It is quite consistent

with physiological laws to have a few of the albuminates slip into the blood, on through the circulation, and out with the urine as albumin, peptones, hemi-albuminose, or some of the many other forms.

Such circumstances as these easily account for the presence of the minute traces of albumin, and in the absence of all the other urinary symptoms, argue strongly against the existence of any organic renal lesion ; it does not in itself prove the approach of an organic renal disease.

In proof of these statements, there are now a fair number of recorded cases of prolonged albuminuria, with no further renal symptoms, which have not terminated in an organic lesion of the kidneys, but on the contrary, in complete recovery. This certainly is strong proof that the simple escape of albumin from the blood through the kidneys does not in itself damage their structure.

The presence of albumin, with the absence of all other renal symptoms, tends to prove that the patient is taking too much albumin, or is unable to completely digest and assimilate the peptones, and completely form serum-albumin. Now if this condition be allowed to pass unnoticed, and without proper treatment, it may become more and more pronounced, nutrition may become decidedly impaired, disease may be developed, and it may be followed ultimately by a giving way of the renal glands. Under such circumstances, the organic lesion of the kidneys is simply the last of a long chain of maladies. A combined study of the physiological and pathological changes in the kidneys tends to substantiate this view. Clinical studies added to these also show how increased work ultimately destroys the normal functions of the renal organs, and finally causes death by the develment of an organic kidney lesion.

On the other hand, there are organic lesions of the kidneys which have persisted for years, and ultimately destroyed the life of the individual, and yet during the whole course of the disease albumin never made its appearance in the urine.

After carefully considering all these circumstances, it seems but just to say that too much stress has been laid upon the recognition of minute traces of albumin as a diagnostic sign of an organic lesion of the kidneys, or of its approach. Certainly, so small a loss cannot produce any strain upon the system, for the simple reason that in the most severe forms of albuminuria the actual amount of albumin rarely exceeds more than three per cent per volume, if it reaches so high a figure. It is well known from experiment that five per cent of serum-albumin in solution will completely gelatinize the fluid upon boiling. If now we compute this loss in comparison with the total volume of

albumin in the blood, and attempt to estimate the total loss to the body per day, it is too small a quantity to be worthy of consideration.

If the percentage of albumin in the urine is not more than 0.004 of one per cent, or 0.008 of one per cent, the loss from the bulk of blood is almost too small to be computed. It may yet be found a most valuable aid as an indicator of a perfect digestion, or one which is incomplete, as well as a guide to the prognosis and treatment in connection with diseases of the hepatic gland and the alimentary tract. The presence of these traces will then come to hold the same relation to these obscure diseases as a more easily recognized quantity bears to the now well understood renal lesions.

(1) *Heat.*—The best method is to fill a test-tube three-quarters full of the urine to be tested. Hold it by the bottom between the thumb and forefinger, and apply the flame of a spirit lamp or Bunsen's burner; heat the upper third gradually to the boiling-point. If no precipitate is formed, it indicates the absence of albumin or the alkalinity of the sample, as serum-albumin readily coagulates at 90° C. 162° F. in acid mediums. If alkaline in reaction, add a drop or two of nitric acid until the solution is distinctly acid. Now, if a precipitate is formed upon boiling, remaining unchanged by the addition of a little more nitric acid, or becoming more decided, albumin is present. But if it remains clear, albumin is absent.

The acid is added for two reasons: first, to dissolve the phosphates, carbonates, and all substances likely to cause a precipitate resembling albumin; and second, to neutralize any alkali that may be present and hinder the precipitation of the albumin by boiling.

Acetic acid is sometimes used instead of nitric acid to acidulate the solution. When acetic acid is used, this important fact should be remembered, in acidulating with this acid while boiling, just enough should be added to neutralize, and no more, for, if rendered decidedly acid, the albumin is held in solution and no coagulation occurs. If, however, the solution is neutralized exactly by the acetic acid, it is one of the most delicate tests.

· From the above reason, that acetic acid may hold the albumin in solution or convert it into an acid albumin which is not coagulated by heat, it has been thought best to render the sample acid by nitric acid before applying heat, but the nitric acid is open to the same objection.

Either of the above will detect 0.018 of one per cent, if not a much smaller percentage.

One of the most accurate methods for detecting albumin is to wash the interior of a test-tube with a four-per-cent solution of acetic acid,

then nearly fill the tube with the urine, and heat the superior third to the boiling point while holding it by the inferior extremity. In this way, if albumin be present, the superior layer will become cloudy while the underlying layer remains clear; in this way a sharp distinction can be drawn, and the merest trace of albumin detected.

It occasionally happens that the natural acidity of the urine is so great that the alkaline serum-albumin is converted into an acid albumin, which is not coagulated by heat. In such instances the urine should be rendered decidedly alkaline by caustic soda or potassium, and then neutralized or made faintly acid by the addition of a four-per-cent solution of acetic acid, and boiled, when the albuminous precipitate will be quite positive.

(2) *Acidulated Potassium Ferrocyanide.*—Acidulate the urine strongly with acetic acid, then add several drops of potassium ferrocyanide. If the solution contains albumin, a white, flocculent precipitate will be developed. It is said that if albumin be less than one-half to two per cent, this test shows no reaction (Thomas). On the other hand, in Dalton's "Physiology," he says: "This is one of the most delicate tests for the presence of albumin." Here certainly are two contradictory statements. If the former be true, it is absolutely worthless in urinary analysis, for only in exceptional cases does the urine reach one and a half per cent.

(3) *Acetic Acid and Sodium Sulphate.*—Acidulate the urine strongly with acetic acid; add one drachm of the strongly acid urine to one drachm of a strong solution of sodium sulphate and boil. If any form of albumin is present, a permanent precipitate will be the result. This test is very exact, and does not produce any decomposition of other bodies which may be present, and hence the filtrate may be further analyzed.

The three following are considered very delicate tests for traces of albumin in solution:

(4) *Caustic Potash and Copper Test.*—Pour one or two drachms of the urine into a test-tube, add a drop or two of a five-per-cent solution of cupric sulphate, and add some liquor potassæ; an excess of the potash does not interfere with the reaction. A precipitate may fall, but it will be dissolved on shaking the tube, and the liquid will assume a violet color. Boil the solution; no precipitate falls, but the violet color will become deeper.

(5) *Xanthoprotein Reaction.*—Add to the sample of urine some concentrated nitric acid, and boil. Let the liquid cool, and then add some ammonia. If the solution contains albumin, an orange color will be produced.

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(6) *Millon's Reaction.*—Add to one drachm of urine (3.887 c.c.) ten minims of Millon's reagent, and heat. If the sample contains albumin in considerable quantities, a white precipitate will fall which will become red when heated. If only a trace of albumin be present, no precipitate is formed, but the fluid becomes red. The red color is produced at ordinary temperatures, but it is increased by heat.

Millon's Reagent is prepared by adding one drachm (3.887 grams) by weight of nitric acid (specific gravity 1.042) to one drachm (3.887 grams) by weight of pure mercury. Dissolve the mercury in the nitric acid at first without, and afterwards with gentle warmth. Add to this solution twice its volume of distilled water; let it stand for some hours, and decant the supernatant fluid from the crystals that have formed at the bottom. Keep in a glass-stoppered bottle.

(7) *Heller's or the Nitric Acid Test.*—Pour one drachm (3.887 c.c.) or a smaller quantity of nitric acid into a test-tube, then hold it obliquely and drop the urine in from the bottle, or by the aid of a medicine dropper or pipette, until an equal volume has been added without agitation. The urine, being of less density, will naturally float upon the top of the acid. At the line of junction of the two liquids, all urinary samples will give a brownish-color line which will vary in intensity with the condition and amount of coloring matter and urea present.

This peculiar ring of color has been considered to be the result of the action of the acid on the coloring matters of the urine. Others hold that it is in some way influenced by the formation of the nitrate of urea, or it may be due to this formation of urea with the property under these circumstances of taking up the coloring matter, as is the case with uric acid in urine.

The only objection to this last theory is that when the crystals of nitrate of urea are formed in abundance at this border line, as occasionally happens, they can be easily taken up by a pipette, mounted upon a slide, and examined under the microscope. They are then found to be devoid of all color, and are nothing but pure white crystals. After they have all been removed by the pipette, or allowed to fall to the bottom of the tube, the color band still remains.

By others, it is held that this color band is due to the deposition of acid urates, and it is also asserted that it is due to the formation of hydrated uric acid. If the color band fell to the bottom with these crystalline and solid substances, these theories might hold; but this change appears to be the result of the action of the nitric acid upon the coloring matter.

When the color line is not very marked and no cloud forms, and albumin is present, a decided, delicate, and perfectly white band is formed on the surface of the acid between the two solutions. If the urine is high colored and loaded with urates, a trace of albumin may be obscured by them, or it may lead to the belief that the whole band is albumin, and that it may be indicative of large quantities. This difficulty may be, in a measure, obviated by gently heating the solution, when the urates will disappear and the white film of albumin become somewhat more distinct.

Heller has advised the use of a somewhat larger dish, with slanting edges, instead of the test-tube. The urine flowing out upon a larger surface gives a more marked reaction.

Hoffman and Ultzmann have advised boiling the urine with an equal bulk of officinal liquor potassa, and filtering. If still not quite clear, add a few drops of the "magnesian fluid" (the magnesian fluid is made by dissolving magnesium sulphate and pure ammonium chloride, each one part, in eight parts of distilled water and adding one part of liquor ammoniæ), warm again, and filter. This test will detect very small quantities of albumin.

(8) To get rid of the two troublesome bands, Dr. A. W. Abbott, of Minneapolis, recommends the following plan: Pour a few drops of urine gently down the inside of a glass vessel containing acidulated water at the boiling point. If albumin be present, a more or less delicate film will form just at the dividing line between the fluid tested and the clear water. This test is said to detect one-twentieth of one per cent.

(9) The following test has been found to work very well, and to obviate most of the difficulties experienced with Heller's method except as modified by Hoffman and Ultzmann:

Pour one drachm (3.887 c.c.) of chemically pure nitric acid into a clean test-tube, then carefully add one-halfdrachm (1.942 c.c.) of distilled water. Both solutions will remain perfectly clear and separate if carefully added, but a distinct line of separation between the two will be easily appreciated on account of the difference in density between the two solutions. Next draw up a little of the urine to be examined in a pipette and allow it to flow down the test-tube, which is to be held erect and not inclined. The suspected solution passes quickly through the water, which acts as a filter, and strikes against the acid suddenly, when a pure white film or layer of coagulated albumin will shoot across the surface of the acid to the opposite side. The thickness of the precipitate will depend upon the amount of albumin present. On account of the perfect transparency of the acid

and water, if the tube is held against a dark background, the faintest film can be detected separating the two fluids.

If the urine be high-colored or loaded with urates, it should be diluted until almost colorless. In this way the deep color line and the cloud produced by the urates, when acted upon by the acid, that so often obscures the albumin in Heller's test, is almost completely overcome, and the albuminous precipitate remains sharply outlined.

This method is much more delicate than Heller's. Its exact delicacy has not been determined. After Heller's and the heat and acid tests fail to show evidence of albumin, the sample can be diluted many times more, and a sharp reaction will follow its application.

This method is very simple, and if carefully followed is free from error. The reason for the precipitate being so positive is the clearness of the two solutions and the precipitation of all the forms of albumin.

(10) *Roberts' Acid Brine Test.*—The principle of this test is the same as when the acetic acid and sodium sulphate are used, a different acid and salt being employed.

A standard test solution is made by adding one ounce (31.103 c.c.) of dilute hydrochloric acid (U. S. P.) to fifteen ounces (466.552 c.c.) of a saturated solution of sodium chloride.

This test is used in the same way as Heller's nitric acid. One drachm (3.877 c.c.) of the brine is poured into a clean test-tube, and the urine allowed to run slowly down the tube so as to prevent undue agitation of the two fluids and an intermingling. If albumin be present in the sample, a white film or layer of coagulated albumin will be found, varying in thickness with the amount present in the sample.

The advantages ascribed to this test are: (*a*) As a rule no color line is formed, and if any, it is slight; (*b*) that it can be carried with less danger than nitric acid; (*c*) it does not stain the fingers; (*d*) it does not precipitate the urates; (*e*) it consolidates all forms of albumin, and the sugar test applied after its use is not interfered with.

On the other side, it can be said that it is no more delicate than the heat and less so than the nitric acid tests.

(11) *Picric Acid Test.*—When this acid is added to normal urine, the only change produced is a slight yellow tinge due to the color of the acid, but no precipitate occurs, and the solution remains perfectly transparent. A saturated aqueous or alcoholic solution may be used as a standard test; the former is the one commonly recommended. It may be employed as follows. Pour one drachm (3.877 c.c.) of the standard solution into a test-tube, then add the urine in the same

manner employed in Heller's acid test; a precipitate will form between the two fluids if albumin be present.

As the picric acid has a lower specific gravity than most samples of urine, it is better to pour the urine into the test-tube first, and then add the acid. The same result, however, is obtained in either case.

If the urine is alkaline, the sample must first be strongly acidulated with acetic acid. In fact, a little acid had better be added in all cases. If the urine is turbid, it should be boiled with one-fourth its volume of liquor potassæ, and then strongly acidulated and tested as before.

This test gives the same kind of a precipitate with the salts of potash as with albumin. It also precipitates all forms of albumin as well as serum-albumin. The application of heat will cause a disappearance of the precipitate with some of the albumins and the potassium salts.

Taken as a whole, there is some uncertainty in relation to the reliability of this test.

(12) *Tanret's or the Potassio-mercuric Iodide Test.*—The test solution is made as follows:

Iodide of Potassium, .	49.68 grains	3.219 grams.
Bichloride of Mercury,	20.83 grains	1.349 grams.

Distilled water, a sufficient quantity to make 3.21 ounces (99,843 c.c.).

It is employed as follows:

(*a*) Boil the urine to be tested with liquor potassæ, and filter.

(*b*) Acidulate the filtrate with citric or acetic acid; the former is most strongly recommended.

(*c*) Add a few drops of this standard solution to the acidulated urine. If only a trace of albumin be present, a slight turbidity is all that can be detected. When the quantity of albumin is large, a decided cloud results. If it is abundant, a very decided precipitate will be produced. The cloud resembles that which occurs when the phosphates are thrown down by heat. If employed in the same manner as the nitric acid test, the two solutions will be separated by a bluish disk of albumin, varying in thickness according to the quantity contained in the sample.

When only a small quantity is suspected, pour one drachm (3.877 c.c.) of the test solution into a test-tube, and add the urine drop by drop until an equal volume has been added. A color disk will form between the two solutions that will be either bluish-white, bluish-yellow, or bluish, depending upon the amount of albumin present.

This test, like most of the preceding, precipitates the peptones, he alkaloids, the urates when abundant, and forms a cloud when

mucus is present. All, however, disappear when heat is applied. This test requires time and some little skill in order to obviate all the possible sources of error, consequently it cannot be considered as practical for general use as the heat and nitric acid tests.

(13) *Oliver's or the Sodium Tungstate Test.*—This substance, like most of the other tests, is used after the manner of Heller's.

The standard test solution is made as follows: Prepare a saturated solution of sodium tungstate, one part in four of water, add a saturated solution of citric acid, ten parts to six of water. Add together equal quantities of the two, and it is ready for using. The urine or the test solution may be poured into the test-tube first, followed by the one remaining. It is a very sensitive test, and said to be free from all objections. Further trial, however, may prove that it precipitates other substances, the same as the foregoing.

(14) *Pavey's Test Pellets.*—This test consists in using little pellets instead of solutions. They are more easily carried. They are composed of sodic ferrocyanide, and are acidulated with citric acid. One of them is crushed and placed in the bottom of a test-tube, and a little urine added, or the urine can be first poured into the test-tube, and the powdered pellet dropped into the suspected solution. This test will produce the precipitation of albumin without the application of heat.

Oleo-resins act in the same manner.

(15) *Test Papers.*—These have been recommended by Dr. Oliver, of Harrowgate, on account of the ease of transportation and their certainty of action. They are prepared as follows: Chemically inert filter paper is soaked, either in double iodide of mercury, sodium tungstate, or ferrocyanide of potassium, allowed to dry and then it is cut into slips of suitable size. Papers charged with citric acid are prepared in a similar manner.

If the urine be turbid, it should be boiled with liquor potassæ and filtered; if clear, this need not be done. In either case the acid papers are added until a decided acid reaction is obtained.

Having accomplished this, one of the first-named test-papers is held in the urine. If only a trace of albumin be present a cloud will form around the test-paper, but if more abundant, a decided cloud will be formed, and the coagulated albumin will fall gradually to the bottom of the tube.

These papers are said to be very delicate, and to give evidence of albumin when heat and nitric acid fail.

It appears as if bedside testing of urine has been very much overesti-

mated. For a complete chemical and microscopic analysis is absolutely necessary, if anything like accuracy in diagnosis is essential.

(16) *Carbolic Acid Test.*—This acid has been recommended to be used in the same manner as Heller's nitric acid test. But the sources of error are numerous, which renders it impracticable.

The exact nicety of a number of these tests have been given by Dr. G. B. Fowler, of this city, as follows:

Heat and acidulation, . . .	.018 of one per cent.	
Acidulated brine, . . .	.018	" "
Picric acid, ...	.008	" "
Nitric acid, ...	.008	" "
Potassium ferrocyanide and acetic acid,	.008	" "
Potassio-mercuric iodide, . .	.004	" "

In all cases the test-tube and its contents should be viewed by reflected light against a black background as suggested by Dr. John P. Munn, of this city.

Instead of using an ordinary test-tube, take a conical test-glass and fill it two-thirds full of the test solution to be used. Then add the urine very carefully to the test solution in the glass, so that it may flow out upon this broad surface and not mingle with it. In this way a large precipitation is likely to be the result, and its presence is more easily detected.

The tests which experience has proved to be the most satisfactory are the heat with acidulation by acetic or nitric acid, the nitric acid alone, with an equal volume of water as recommended in the text, the xanthoprotein reaction, and the acid brine test.

The acid brine and nitric acid tests are both very ready methods for estimating the amount in a volumetric way. If, for instance, the albuminous precipitate occupies one-half of the fluid above the acid or the brine, it may be said to indicate fifty per cent; if only one-fourth, twenty-five per cent. As a comparative test from day to day, this is quite a practical method, but in reference to the actual percentage of albumin contained in a given specimen, it is, like all the other tests recommended, absolutely inaccurate.

The only method by which anything like accuracy can be obtained in estimating the quantity is by the gravimetric method. This consists in the precipitation of the albumin upon a weighed filter, and then deducting the increase in the weight of the filter from the total weight of the urine from which the albumin was precipitated. The only source of error in this method that cannot easily be avoided is the precipitation of a small amount of coloring-matter and the earthy phosphates along

with the albumin. As most of the coloring matter and phosphates are removed by thoroughly washing while on the filter, this error is not sufficiently great to be considered. The method is of no practical value to the general practitioner from the fact that it requires a large amount of delicate apparatus, and also takes considerable time and skill to arrive at an accurate result.

There are a large number of methods offered by different writers, all of which appear to be too complicated and uncertain to be absolutely practical. They will be named and the references given only. By circumpolarization; the method of Bödeker; Vogel's optical method, Lang, Haebler, and Bornhardt Méhu's method, method of P. Liborius, L. Girgensohn's method, W. Roberts' dilution method.

As the actual quantity lost is so small, the knowledge of the loss being $\frac{1}{1000}$ or $\frac{1}{100}$ more or less, is of no practical value in relation to the symptoms, prognosis, or treatment. The volumetric analysis in the test-tube from day to day is certainly a very sure index of the rise and fall in the quantity of albumin and gives all the information required.

Clinical significance.—The first thing to decide is whether the albuminuria is of the adventitious or intrinsic variety. This can be accomplished by exclusion. If the albumin persists without any further evidence of structural change in the kidneys it is reasonable to suppose that it is of the adventitious form. The absence of serum-albumin and the detection ·of the peptones or some of the derived albumins in abundance would confirm the diagnosis.

If, on the other hand, the serum-albumin predominates, with casts and other evidences of a structural lesion of the kidneys, the albuminuria is of the intrinsic variety.

Prognosis.—This of necessity depends upon the kind of albuminuria. In the adventitious, if its cause can be removed, the prognosis is good, otherwise it may terminate in the intrinsic variety.

In inherent albuminuria, the prognosis also depends largely upon the cause. In connection with the fevers, acute and chronic metallic poisoning, and the acute renal lesions, recovery is possible and not infrequent, but in connection with chronic venous obstruction or in a well-established renal lesion the prognosis is always bad.

Treatment.—This is exclusively confined to the removal of the causes. In the adventitious variety, if due to the abstinence from sodium chloride, it should be added to the diet; if due to imbibing too much egg-albumen, the quantity taken should be diminished; if to a faulty intestinal or hepatic digestion, this should be overcome.

The treatment of the intrinsic variety has been covered in treating of the various renal lesions in which it occurs.

The adventitious variety will often disappear under the influence of the bile pill and the nerve tonic composed of nux vomica and damiana, see pages 26 and 89. The diet should always be of the albuminous type and limited to those substances most easily and completely digested and assimilated.

CHAPTER IV.

GLUCOSE OR GRAPE SUGAR. TESTS FOR GLUCOSE.

Sugar.—Glucose is found in the urine in the condition known as glycosuria or diabetis mellitus. It also occurs as the result of poisoning by urari, carbonic oxide, with a sufficient dose of morphia and amyl nitrite. It has also been met with in ¹disturbances of the medulla or base of the brain, occasionally in health and sometimes after surgical operations. A trace of glucose is said to be normally present both in the blood and urine, but since the observations of Prof. Satterthwaite, who found that both uric acid and kreatin caused the same reaction with the glucose tests as sugar, it is quite possible that this may not be true.

A large number of tests have been suggested from time to time.

They are, *first, Moore's* or *Heller's.*—To one drachm (3.887 c.c.) of urine add an equal quantity of caustic soda or potassa, and boil. If glucose be present, the mixture will at first turn to a light yellow, then to an amber color, and lastly to a dark orange-brown color.

This, however, is an uncertain test, as many other organic compounds frequently found in the urine cause the same discoloration under similar circumstances.

Second, Trommer's.—Take one drachm (3.877 c.c.) of urine and add 12 minims of a 12% solution of cupric sulphate (℥ i. to ℥ i. 3.877 to 31.103 c.c.) so that a very slight green color is perceptible, then add to the solution one and one-half drachms (5.831 c.c.) of liquor potassæ. The previously formed precipitate of the hydrated copper oxide will now be dissolved and the fluid will assume a rich blue tint. Now gradually heat; before precipitation occurs, the fluid becomes opaque and presents a yellowish-red color, but after boiling for a few seconds an abundant precipitate of cuprous oxide is deposited ; if sugar be present, the precipitate is of a brick-red color.

The same reaction will take place without the application of heat and is then called *Cappezzuole's test.* In this way the reaction does not occur for half an hour or more.

If Trommer's test is employed in the way above described, it will be

found one of the most accurate, if not the most certain method for detecting the presence of the glucose. It has been stated that this would not reveal the presence of sugar in albuminous solutions, but this has been found to be erroneous.

The following experiments performed by Prof. Satterthwaite, and which, never having been published, are, by his permission, given in detail, are interesting in showing the accuracy of this test, provided the above stipulated quantities be used as recommended by him.

Experiment 1.—With reference to copper test for sugar in albuminous solution. Took a 5% serum-albumin solution to start with. 20 ♏ (1.295 c.c.) of this 5% solution were poured into a test-tube, and 2 ♏ (0.129 c.c.) of a glucose solution added, then 4 minims (0.291 c.c.) of a 12% sulphate of copper solution (℈ i. to ℥ i.) and 30 minims (1.943 c.c.) of liquor potassæ added and boiled. At first the reaction was doubtful, the fluid turning greenish, then yellow by direct light, but at the end of five minutes the reaction was good.

With such a large percentage of albumin, the fluid is apt to gelatinize and become practically solid upon boiling.

Experiment 2.—This was the same as Exp. 1, except that a 2½% solution of albumin was used instead of the 5%. The reaction in this case was immediately sharp and satisfactory.

Experiment 3.—Trommer's test was applied to a simple aqueous solution, which contained only one grain of glucose to the ounce. To 20 minims (1.295 c.c.) of the dilute solution 4 minims (0.291 c.c.) of a 12% copper solution, and 30 minims (1.943 c.c.) of liquor potassæ were added and boiled, and it gave a clear brick-red color with a slight deposit.

Experiment 4.—Took 20 minims (1.295 c.c.) of a saturated solution of uric acid. 4 minims (0.259 c.c.) 12% of the copper solution, and 30 minims of liquor potassæ. The brick-red copper deposit was thrown down after boiling the solution for ten minutes.

Experiment 5.—Took 20 minims (1.295 c.c.) saturated solution of kreatin, 4 minims (0.295 c.c.) of the 12% copper solution, and 30 minims (1.943 c.c.) of liquor potassæ. The deposit of reduced copper was not thrown down until the solution had been boiled for seven minutes, and then it was reddish-green.

Experiment 6.—Took 20 minims (1.295 c.c.) of a saturated solution of tannic acid, 4 minims of the 12% copper solution, and 30 minims (1.943 c.c.) of liquor potassæ. A reddish deposit was thrown down, the color being a sealing-wax red.

Experiment 7.—To a 5% solution of serum-albumin one grain (0.064

c.c.) of glucose to the ounce (31.103 c.c.) was added. Took 20 minims (1.295 c.c.) of this saccharated and highly albuminous fluid, and added 4 minims (0.295 c.c.) of the 12% solution of copper, and 30 minims (1.943 c.c.) of liquor potassæ, and boiled. The characteristic color reaction of Trommer's test occurred, but no precipitate fell.

Experiment 8.—Took 20 minims (1.295 c.c.) of the same saccharated albuminous fluid and applied Fehling's test. Reaction obtained, but less perfectly than by the use of Trommer's.

Experiment 9.—Took 20 minims (1.295 c.c.) of a saturated solution of hippuric acid, 4 minims (0.259 c.c.) of the 12% copper solution, and 30 minims (1.943 c.c.) of liquor potassæ. No reduction of copper was produced.

Dr. Samuel Lloyd has noticed,[1] in a series of examinations of diabetic urine by Trommer's test, that when no precipitate had occurred during the boiling, a flocculent white deposit took place during the cooling if the specimen contained little sugar, but an excess of the urates and phosphates. This led him to make a number of experiments to determine the accuracy of the test. Specimens containing urates, phosphates, and sugar only were each submitted to the test according to the usual method, a small quantity of the urine being poured into a test-tube, and then a drop or two of the sulphate of copper solution and excess of the soda or potash solution. The result was the same with the specimens containing the phosphates and the urates, but with the sugar solution the characteristic color was observed. Solutions were then prepared which contained large quantities of the other two ingredients, but very little sugar, and it was then found that the color imparted to the supernatant fluid by this one substance was sufficient to serve to color the entire precipitate, and thus lead to the erroneous conclusion that the whole heavy deposit was suboxide of copper, due to the presence of sugar, and that the patient must necessarily be well advanced in the disease. He had finally concluded that, if this test was used, the phosphates should first be precipitated by heat, and the urates neutralized by adding the soda before the copper.

From this it would appear that if Trommer's test is used in the above proportions, it still holds the first place for detecting sugar in the urine. The difficulty heretofore experienced with it appears to have come from no definite quantities having been laid down as the standard to work with.

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[1] New York Medical Journal, March 14th, 1885, p. 313.

The other substances which occur in the urine and are capable of reducing the copper require several minutes' boiling to effect this reduction, but with glucose it is almost instantaneous, and in this way it can be distinguished.

Third, Fehling's Test.—This has heretofore been said to be a more delicate copper test than that of Trommer. A number of formulæ and modifications have been advanced. *First:*

Pure crystallized sulphate of copper, .	500 grains.
Neutral tartrate of potassium, . .	2,000 "
A solution of caustic soda of a specific gravity 1.12, ...	8,750 "

The neutral tartrate of potassium, dissolved in a little water, is first mixed with a solution of caustic soda. Then the sulphate of copper dissolved in about $4\frac{1}{2}$ fluid ounces of water, is gradually added to the alkaline liquor, which assumes a deep blue color. The whole is diluted with water to the volume of $31\frac{5}{8}$ fluid ounces. About $\frac{1}{4}$ of a fluidrachm of Fehling's liquor is exactly decolorized by .077 of a grain of glucose. One drop of Fehling's solution will detect about $\frac{1}{1000}$ of a grain of glucose dissolved in about $\frac{1}{4}$ ounce of water.

Second. It is made as follows:

Take Pure crystallized sulphate of copper, .	40 grams.
Neutral potassium tartrate, . .	160 "
A solution of sodium hydrate, specific gravity 1.12, ...	650 "

The further preparation is the same as the above, only using 160 cubic centimetres in place of $4\frac{1}{2}$ ounces of water, and diluting to 1154.4 cubic centimetres instead of $31\frac{5}{8}$ ounces. One cubic centimetre of this solution is exactly decolorized by $\frac{1}{200}$ of a gram of glucose.

Third. Pavey's solution is made as follows:

Cupric sulphate, ...	320 grains.
Neutral potassic tartrate, . . .	640 "
Caustic potash, ...	1,280 "
Distilled water, ...	20 fl. oz.

The solution is made in the same manner as Fehling's, and 100 minims correspond to $\frac{1}{2}$ grain of grape sugar, the formula for grape sugar being here taken $C_6H_{14}O_7$, while by Fehling it is taken $C_6H_{12}O_6$.

Fourth. A modification and method described by Prof. Austin Flint, Jr., is as follows:

"Make a solution in the proportion of 379 grains of neutral tartrate of potash to a fluidounce of distilled water, and keep for use.

"Make a solution in the proportion of 95 grains of sulphate of copper to a fluidounce of distilled water, and keep for use.

"Make a solution of caustic soda in distilled water, of a specific gravity of 1.12 or 16½ Baumé, and keep for use.

"Take half a fluidrachm of the solution of copper, add half a drachm of the solution of tartrate of potash, add of the solution of caustic soda sufficient to make three fluidrachms. Boil the test liquid, and when it is hot, add the urine drop by drop. If sugar be present, the addition of a few drops of urine will produce suddenly an opaque yellowish-red precipitate. If a volume of urine be added, drop by drop, equal to the volume of the test, and the mixture be brought to the boiling point and then allowed to cool without any precipitate, it is absolutely certain that there is no sugar."

Fifth.—A former student and clinical assistant, Dr. John E. Bailey, still further modified Fehling's and Prof. Flint's methods. His also is composed of the three solutions, but instead of taking equal quantities of the copper and neutral tartrate solution and double the quantity of the third or soda solution, an equal quantity of each is taken, which is more easily remembered. The solutions are designated 1, 2, and 3 in the order in which they are to be added, and are made as follows:

Solution I.

Cupric sulphate,	.	47.43 grains, 3.073 grams.
Distilled water,	. .	1 fluidounce, 31.103 c.c.

Solution II.

Neutral tartrate of soda,	236.88 grains, 15.349 grams.
Distilled water, .	1 fluidounce, 31.103 c.c.

Solution III.

Caustic soda,	. .	80.65 grains, 5.226 grams.
Distilled water,	. . .	1 fluidounce, 31.103 c.c.

All three solutions should be carefully filtered. It is very essential in all cases to get a pure neutral tartrate salt, otherwise the test may fail. In using this test, equal quantities of the three solutions are

turned into a test-tube in their numerical order; by so doing no temporary precipitation occurs. The union of these three solutions develops a rich blue color. The further application of the test is the same as recommended for Prof. Flint's.

The use of the neutral tartrate of soda is preferred to the potash salt, experience having taught that it is less likely to fail in albuminous solutions. One hundred (100) minims of this solution are exactly decolorized by one-half a grain of glucose in an aqueous solution, glucose being taken at $C_6H_{12}O_6$.

This solution has been in use in the laboratory of the New York Post-Graduate Medical School and Hospital for a number of years, and it has never been known to fail.

The advantages claimed for Drs. Flint's and Bailey's methods are that the three are kept in separate vials and do not decompose with age, which is often the case with Fehling's. Consequently they are always ready for use, and as diabetic cases are not of every-day occurrence, Fehling's solution is frequently found decomposed when it is most needed.

Sixth. *Dr. E. R. Squibb,* of Brooklyn, has still further modified the test by having only two solutions. Any two of the solutions together will, after a time, decompose and render the test uncertain. The only advantage claimed for Squibb's method is two bottles instead of three.

The three-bottle method is preferred.

Seventh. *Dr. H. G. Piffard's* Cupro-Potassic Paste:

Take of: Sulphate of copper (chemically pure), . . 1 part.
       Crystalized tartrate of sodium or potassium (C.P.), 5 parts.
       Sodic hydrate (chemically pure), . . 2 "
    Mix thoroughly in a mortar.

The result will be a pasty mass, which can be transferred to a wide-mouthed bottle and kept till wanted. *To use it,* take of the mass a piece about the size of a small pea, put it in a test-tube and add about two fluidrachms (7.775 c.c.) of water; boil until the mass is dissolved, and the solution has a uniform, pale, and rather dirty-blue color; then add two or three drops of the suspected urine, and boil again for a moment. If sugar be present, the usual reaction will be manifest.

Eighth. *Boettger's* bismuth test consists in the action of sugar as a reducing agent on bismuth.

First method.—1. Solution of crystallized carbonate of soda; strength, one part to three of distilled water.

2. Ordinary subnitrate of bismuth. Pour one drachm (3.887 c.c.) of the suspected urine into a test-tube, then one drachm (3.887 c.c.)

of the carbonate of soda solution, and add from one to five grains of bismuth. Boil the mixture, and if sugar be present, the solution will first become gray and then black from the deposit of metallic bismuth.

Second method.—Pour into a test-tube one drachm (3.887 c.c.) of urine and one drachm (3.887 c.c.) of liquor potassæ or soda, then add from one to five grains of ordinary subnitrate of bismuth, shake and boil for two minutes; first the play of colors, as in Moore's test, will be observed, then a gray, and finally a black precipitate of metallic bismuth will be developed.

Third method or *Lowe's test.*—It is almost identical with the preceding, the only difference being the addition of a little glycerin and the use of soda instead of potash. The result is the same.

All these tests are open to objections, the bismuth being reduced in like manner by sulphur, albumin, or any substance containing sulphur. As albumin and sugar are frequently associated in the same sample, it is only confirmatory in connection with other tests.

Silver, chromium, uranium, and tin are in a similar manner reduced by the presence of sugar.

Ninth. Maumene's tin test.—To apply this test, pieces of merino or any other woollen fabric are soaked in a solution of bichloride of tin, and carefully dried. On wetting a piece of this cloth in the suspected sample of urine, and then holding it over a spirit lamp or before the fire until it becomes hot, a deep brown or black spot will appear if sugar be present.

Tenth. Brücke's modification of the bismuth test.—Professor Brücke recommends that urine containing any sulphur compound be faintly acidulated with hydrochloric acid and then heated with Frohn's reagent. The reagent is made as follows: Take 23.94 grains (1.5 grams) of basic nitrate of bismuth, and heat to the boiling point with 308.64 minims (20 grams) of water; then add 107 grains (7 grams) of potassium iodide, and 20 minims of hydrochloric acid. This reagent is orange-red in color.

This solution completely removes the sulphur, but does not affect the glucose. It is then filtered and the filtrate boiled for five minutes with an excess of a concentrated solution of caustic potash; if a gray or black color, or a blackish precipitate, is formed, the presence of sugar is proved beyond a doubt.

The test, although quite accurate, is by far too complicated for a ready and practical every-day test. It may occasionally be found of service as confirmation proof in doubtful cases.

Eleventh. Mulder's Test.—Heat to boiling the suspected urine, which

should be colorless, or nearly so, with a solution of indigo-carmine which has previously been rendered alkaline by sodium carbonate, and a change of color is the result. It at first is blue, then green, then purple, and if a large quantity of sugar be present, red, and finally yellow. If this solution, while hot, is shaken so as to allow an admixture with the oxygen of the air, the play of colors will be reversed and returns to blue; but after standing, the yellow color reappears. When the amount of sugar is very small, the indigo-carmine becomes pale-blue only.

This test is said to detect very minute quantities of glucose.

Twelfth. *Fermentation test* consists in the splitting up of glucose into carbon dioxide (CO_2) and alcohol (C_2H_6O). It can be applied by placing some of the suspected urine in a receptacle with a little brewer's yeast. This can be easily applied by taking two bottles, the first of which shall contain the suspected fluid, together with a little brewer's yeast, and closed by a perforated cork conveying a bent glass-tube which is longest in the arm not inserted into the cork. The second bottle should contain lime-water and the long or external arm of the glass-tube should be placed so that its mouth is immersed under the fluid in bottle No. 2. Carbon dioxide (CO_2) will, after a time, be generated and driven off through the tube, and if allowed to discharge into a solution of lime-water a white precipitate of the carbonate of lime will be thrown down. This will establish the presence of sugar beyond doubt, but this is not a very ready and practical test, as it takes about twelve hours for fermentation to be accomplished.

Thirteenth. *Polarization.*—This test consists in the fact that glucose rotates the plane of the polariscope to the right, 56. + or 57.6.

Fourteenth. *Caustic Potash in Alcohol.*—By adding caustic potash in alcohol to a saturated solution, a precipitate of white flakes will be thrown down.

Fifteenth. *Quicklime Test.*—An excess of quicklime added to saccharated urine will cause a precipitate which, when treated with alcohol, forms a white mass.

Sixteenth. *Silver Test.*—Add a weak solution of ammoniated nitrate of silver to the urine, and boil for a time; if sugar be present, metallic silver will be deposited, forming a mirror.

Seventeenth. *Heinzinga Test.*—Add to urine hydrate of potassium, and then a few drops of molybdate or tungstate of ammonium, heat to boiling, then acidulate carefully with hydrochloric acid, there will result, if sugar be present, a blue color.

Among the older methods may be mentioned:

Eighteenth. The *first* method or that of Dr. Cruikshanks. It

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consisted in the addition of nitric acid to urine, which converted the sugar into oxalic acid, throwing it down in crystals. Next came:

Nineteenth. Hünefield's Test.—This test depended upon the reducing power of glucose upon chromium; a strong solution of chromic acid being taken as the standard.

Twentieth. Runge's Test.—A small quantity of urine is evaporated upon a white surface, and while warm a few drops of dilute sulphuric acid are dropped upon the residue. Normal urine will give a pale-orange color; but if sugar be present, a deep brown and ultimately black, owing to the decomposition of the sugar and a deposition of carbon. This test is capable of detecting one part in one thousand.

By almost any of the above enumerated tests, the examiner with a moderate amount of skill can detect the presence of glucose in the urine whenever it exists in sufficient quantity to be of any practical importance. But the tests which are the most practical and freest from error in the hands of all are the modification of Fehling's as arranged by Dr. Bailey, and Trommer's, both of which are strongly recommended as standard test solutions for detecting glucose in urine, as they have all the advantages and none of the disadvantages of the other methods.

The Trommer's to be used in the proportions already given, and not in the indefinite way in which it is often recommended.

Quantitive Analysis of Urine for Glucose.—It has generally been spoken of, as *absolutely* necessary to determine positively the change in quantity of the amount of sugar excreted daily by a diabetic patient. Much has been written in regard to determining the amount of sugar excreted, but as yet no practical necessity has been demonstrated for such precision.

An *exact* determination of the daily quantity of urine voided and the relative change and comparison of the specific gravity will yield a very good result in reference to the change in the amount of glucose excreted from day to day. Although from a chemical point of view it has been spoken of as the older and crude method; clinically and practically, if the quantity and specific gravity be correctly taken, it yields about as reliable information as any of the methods yet introduced. This method has been the most popular with the general practitioner; for up to the present time no more ready, easily manipulated, and practical method has been discovered.

Numerous methods have been advanced, but all, with the exception of Roberts' fermentation test, have been too complicated to be practical, or have depended upon a decolorization of solutions or variations in shades of colors, and estimates based upon these changes. The fallacy

of any quantitive test based upon change or changes in color is apparent, for the reason that few are endowed with the special faculty of accurately distinguishing shades in color, and especially, rapid and delicate transitions in these colors. Again, as these tests are applied to a few minims only of the suspected sample, a wrong judgment in reference to the color must lead to a great error when the computation is made and applied to the large quantity of urine voided daily. In a few minims the fractional error would be small perhaps in the hands of an expert, but in relation to a large quantity the result must be far from accurate. In fact, no two persons are apt to agree in reference to delicate shades or, to say the least, there is often a difference of opinion. In one instance, when several physicians were trying Fehling's decolorization test, they could not agree, some claiming complete decolorization, others the reverse. After allowing the test to stand for a few minutes, however, the blue color became apparent to all, which clearly showed an error in judgment on the part of one of the parties.

A variation of from five to six hundred grains (32.399 to 38.879 grams) per day by different examiners, all estimating the quantity from the same sample by Fehling's method, has frequently been observed.

With still more delicate shades of color as evidence of different percentages, the chance for error must necessarily be very great.

In quantitative analysis in chemistry, unless it is absolutely accurate, it is considered valueless. The same ought to hold true in practical medicine.

It is undoubtedly quite possible for an expert with all the laboratory conveniences and repeated practice to obtain very close results with any one of the methods advocated, but it cannot be expected from the general examiner, and the sooner this view is adopted the better.

Roberts' fermentation test is based upon the fact that diabetic urine loses density by fermentation.

The test is employed as follows: Take four ounces (124.413 c.c.) of the urine to be examined, and pour it into a twelve-ounce bottle and add a lump of German yeast as large as a walnut. A little more or less does not appear to materially alter the result. The bottle is then corked with a perforated stopper to permit of the free escape of the carbon dioxide (CO_2), and set aside in a moderately warm and uniform temperature. An equal quantity of the sample is kept in a tightly-corked bottle for a comparison of specific gravity. At the end of twenty-four hours, or forty-eight at the outside, fermentation will be

completed, and the density found to have fallen. Every degree of loss is said to be equal to one grain of sugar to the ounce. By multiplying the number of degrees lost, or the number of grains per ounce, by the factor 0.23, the percentage is calculated.

Provided this test was absolutely accurate, it would be a very good one, and the only objection then that could be raised against it would be the time needful to obtain the result.

In experimenting with this test in solutions of known strength, the discrepancy has often been very great; in one instance as large an error as seventeen per cent was the result, and an accurate analysis was never secured.

Since experimenting with the test, it has been found that an accurate result may be obtained provided the quantity of yeast used is rightly judged, and the fermentation kept at an even temperature, and the urinometers used are very accurate, but experience has led to the belief that it is not certain and accurate under ordinary circumstances.

With this, as in all quantitative tests, applied to the urine, a positive knowledge is required not only of the changes in the urine, but of the quantity of sugar-producing elements ingested daily.

The old method, therefore, of measuring the quantity passed daily and observing the changes in specific gravity yields about the same results, and certainly is far more practical.

The quantitative and qualitative test for glucose as given by Max Enhorn [1] is as follows. His article is quoted in full.

"Now, inasmuch as fermentation is not only the most exact, but also the *only* test for sugar in the urine, the desire of bringing it more into practical use seems to be justifiable. The object of this paper will be to simplify, as much as possible, the method of making the test, and to increase the value of it by enabling us to ascertain at the same time the approximate quantity of sugar.

"Before proceeding with the proposed theme, I will give a literal translation of the method of carrying out the fermentation test, as it appeared in my original article: [2]

"The test apparatus for this purpose is a fermentation-tube, and the most convenient form is that which is described by Salkowski and Leube. [3] It is made of glass, and consists essentially of four parts: (*a*) a spherical reservoir, open at both ends; (*b*) a cylindrical tube, closed at its upper end; (*c*) a somewhat narrower tube, bent so as to connect

[1] New York Medical Record, January 22d, 1887, p. 91.

[2] Virch. Arch., Bd. 102, p. 268–270.

[3] Salkowski and Leube: "Die Lehre vom Harn," p. 223.

(*a*) and (*b*); (*d*) a stand to support the other parts.   A small piece (one gram) of fresh commercial compressed yeast is thoroughly shaken in a test-tube with about ten cubic centimetres of the fluid to be examined, and the spherical reservoir is filled with the resulting mixture. By inclining the apparatus, the mixture easily finds its way through the connecting-tube into the cylinder, completely driving out and replacing the contained air.   Owing to the atmospheric pressure exerted on the reservoir end of the connecting-tube, the fluid does not flow back, but remains in the cylinder and tube.   A little mercury is now poured into the reservoir; it sinks into the connecting-tube, forcing the fluid which was in the latter back into the reservoir.   The cylinder is now filled with the fluid to be tested, and is shut off from the air by means of the mercury.   It is evident that if alcohol fermentation sets in, carbonic acid gas will be evolved, and, displacing the fluid in the upper part of the cylinder, will force it back into the reservoir.   The apparatus is left undisturbed at a temperature of about 30 to 33° C. (86 to 92° F.) for twenty to twenty-four hours.   The changed level of the fluid in the cylinder shows that the reaction has taken place.   The upper part of the cylinder is filled with carbonic acid gas.   To carry out the test as suggested by Salkowski-Leube, three of these fermentation-tubes are necessary.   Of these, A [1] is filled with the mixture of yeast and normal urine, free from sugar; B with the mixture of yeast and the suspected fluid, and C with a mixture of yeast and a urine to which sugar has been added artificially.   (C is used simply to test the efficacy of the yeast.)   Now, should the fluid have been forced out of the upper part of the cylindrical tube B, and its place taken by gas, while in A there is only a small bubble at the summit of the tube, then B contains sugar.   If this is not the case, *i. e.*, if B contains merely a gas bubble similar to the one in A, while C, on the other hand, is partly filled with gas, then, obviously, B contains no sugar.

"Being familiar with this method of carrying out the fermentation test, let us examine the first point of our theme, which has for its object the simplification of the method.   In the above description it was said that, after having filled the fermentation-tube with urine and yeast, mercury must be added—in this way the cylindrical part of the tube is separated from the reservoir and the air.   Moreover, the test is made at a temperature of 30 to 33° C., because this degree of heat affords the best conditions for fermentation.   The necessity of a defined temperature and the addition of mercury are two conditions

[1] The letters A, B, C, etc., signify the fermentation-tubes filled with the different fluids to be examined.

which, though they may be easily carried out in a labarotory, cause, nevertheless, some difficulties to a practical physician. Accordingly I considered the following two questions: 1. Is the defined temperature (30 to 33° C.), which is the most applicable for the fermentation process, absolutely necessary, *i. e.*, would not the ordinary temperature of the room give us a result sufficiently accurate? 2. Is a separation of the urine from the air absolutely necessary, and if so, can we not separate them by something more convenient than mercury?

" In order to ascertain whether the ordinary temperature of the room would be suitable for the test, I made the following two experiments:

" *Fermentation test at the ordinary temperature of the room.*—1. April 23d, 1886: A, urine, acid, 1.034, sugar; B, urine, acid, 1.020, sugar; C, urine, acid, 1.022, no sugar. After two hours: A, the cylindrical part of the tube empty; B, nine-tenths of the cylinder empty; C, a very small bubble at the summit of the tube. April 24th, 1886: A, no fluid in the cylinder; B, fluid to the depth of about two lines in the cylinder; C, three small bubbles on the top of the tube.

" 2. May 8th, 1886: A, urine, acid, 1.022, sugar; B, urine, acid, 1.024, sugar; C, urine, acid, 1.034, sugar; D, urine, acid, 1.010, no sugar; E, urine, acid, 1.020, no sugar; F, urine, acid, 1.024, no sugar. After one hour the sugar reaction in A, B, and C is very apparent. May 9th, 1886: A, seven-eighths of the cylinder empty; B, three-eighths of the cylinder empty; C, eight-ninths of the cylinder empty; D, E, and F, a small bubble on the top of the cylinder.

" Both experiments clearly show that the alcoholic fermentation takes place even at the ordinary temperature of the room, and thus demonstrates, by the large amount of gas, the sugar reaction. Further, we see here also in the urines not containing sugar a small bubble at the summit of the tube, but this bubble is smaller than that produced at 92° F.

" In a word, the fermentation test can be used in the ordinary temperature of the room.[1]

" To determine the second question, whether a separation of the test-fluid by mercury or another substance (as oil) is absolutely necessary or not, the following experiment was made:

" May 9th, 1886.—A, diabetic urine, acid, 1.034, plus mercury; B, diabetic urine, acid, 1.034, plus oil; C, diabetic urine, acid, 1.034, without mercury and without oil; D, normal urine, acid, 1.018, plus

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[1] I have made the fermentation test during summer and winter in my room; the temperature varied from 65 to 85° F.

mercury; E, normal urine, acid, 1.018, plus oil; F, normal urine, acid, 1.018, without mercury and without oil. After one hour: A, B, and C, plain sugar reaction. May 10th, 1886.—A, B, and C, the whole cylinder empty; D, E, and F, a bubble on the top of the cylinder.

"Thus it clearly appears that the addition of mercury or oil has no influence on the reaction.

"The above-mentioned experiments showed that the fermentation test could be used at the ordinary temperature of the room and without any addition of mercury or oil, but still it was a question whether the minuteness of the reaction had not been lessened in a high degree by this simplification.

"Starting from this point of view, I took specimens of the urine of twelve healthy people, and made with them all the fermentation test; to one of these specimens I added a little of a grape-sugar solution, so that the urine contained one-tenth per cent of sugar; then this urine was also examined by the fermentation test:

"June 4th, 1886.—A, urine, acid, 1.020, no sugar; B, urine, acid, 1.016, no sugar; C, urine, acid, 1.024, no sugar; D, urine, acid, 1.022, no sugar; E, urine, acid, 1.020, no sugar; F, urine, acid, 1.024, no sugar; G, urine, acid, 1.022, no sugar; H, urine, acid, 1.026, no sugar; I, urine, acid, 1.026, no sugar; K, urine, acid, 1.026, no sugar; L, urine, acid, 1.025, no sugar; M, urine, acid, 1.018, no sugar; N= urine I, 10 c.c. mingled with 0.2 c.c. of a five-per-cent grape-sugar solution, therefore the urine N had one-tenth per cent of sugar (here the sugar could not be detected by Fehling's test). June 5th, 1886.— A, B, C, D, E, H, I, L, and M, a small bubble (0 0); F,=0; G and K=0; N,=one-tenth c.c., empty.

"Thus we see by this experiment that the amount of gas at N (i. e., in urine containing one-tenth per cent of sugar) was much larger than in the other twelve normal specimens, and that it was in this way possible to recognize with accuracy the presence of sugar.

"I intentionally took this large number of specimens of normal urine, because the size of the gas-bubble in normal urine varies in a certain degree,[1] and I thus learned that the quantity of gas produced in the cylinder by urine containing one-tenth per cent of sugar is much larger than the largest gas-bubble in urine not containing sugar. Therefore it is evident that the delicacy of the fermentation test is not much lessened by the simplification; for even in a temperature of 92° F., and with mercury, we are able to discover the presence of only one-tenth per cent of sugar in a urine that has not been boiled.

[1] These variations usually depend upon the degree of concentration of the urine by salts, as the bubble becomes larger in more concentrated urine.

" As to the time elapsing before the beginning of the fermentation, I could recognize the arising of the first gas-bubbles after fifteen to twenty-five minutes.   Thus urine containing not too small an amount of sugar will show the reaction even at that early time.

" As regards the number of the fermentation-tubes necessary for a test, it is sufficient to take two (instead of the three above mentioned): one (A) with normal urine, the other (B) with the suspected urine. Whether the yeast is good or not we can see by the developed bubble in A: for if the yeast be bad, no bubble will be in A; and should the yeast contain sugar, then we should see in A a large displacement by gas.

" All experiments I shall quote hereafter have been made in the ordinary temperature of the room and without the addition of mercury.   I mention here this fact in order to avoid repetitions.

" I shall now take up the second part of my theme, namely, how to ascertain the quantity of sugar by my fermentation test.

" Two methods of ascertaining the quantity of sugar by fermentation have been used.   One, called 'chemical,' consists in weighing a definite quantity of urine before and after fermentation; the difference of weight caused by the escaped carbonic acid gas gives the quantity of the changed sugar.   The other, called 'clinical,' suggested by Roberts, consists in the difference of the specific gravity of the urine before and after the fermentation process.

" In the following I shall try to make use of the carbonic acid gas space developed in the cylinder of the fermentation-tube to ascertain the proximate quantity of sugar in the urine, a method which has hitherto been used to detect merely the presence of sugar.   Supposing I succeed in this point, then the fermentation test, as I make it, would gain much in value; for it would not only show the presence or absence of sugar in the urine, but it would also give an idea of the quantity of sugar present.

" If the fermentation-tube were constructed in such a way that the whole quantity of carbonic acid gas, developed by the alcoholic fermentation of the urine containing sugar, would gather in the cylinder, then it would be easy to conclude from the development of the gas volume at a given temperature and degree of barometric pressure the exact quantity of sugar.   But this is not the case, for as soon as some carbonic acid begins to gather on the top of the cylinder, a corresponding quantity of fluid is pressed from the cylinder into the reservoir.   The carbonic acid developed in the reservoir escapes from the surface of the fluid into the air.   Thus the gas volume of the cylinder does not represent the whole quantity of gas generated, for

it lacks the carbonic acid which is developed in the fluid driven into the reservoir. Although the gas volume of the fermentation-tube does not correspond to the whole quantity of evolved carbonic acid, it is nevertheless always larger or smaller, according to the greater or smaller quantity of sugar in the fluid.

"It is probable that a fluid containing a certain quantity of sugar would evolve in the fermentation-tubes—as they are all of the same size—equal volumes of carbonic acid gas. If this be the case, then we could determine by experiment the gas volumes of fluids containing certain percentages of sugar, and from this would be able to conclude, from a certain developed gas volume in the cylinder, the quantity of sugar.

"In order to be able to state easily the quantity of the gas volume in the tubes, I graduated the cylindrical part (containing six cubic centimetres) in cubic centimetres and fifths of a cubic centimetre. In this way the quantity of the gas volume can be read from the cylinder. The idea that one and the same sugar solution must reproduce in the tubes equal gas volumes has been verified by experiments. I found only small variations of two-fifths to three-fifths of a cubic centimetre, and they depend probably upon the differences in temperature and barometric pressure. In order to make the test not too complicated, I intentionally did not take the temperature nor the barometric pressure into consideration.

"The following tables show the quantity of developed gas volumes in specimens of urine containing definite percentages of sugar. To determine these quantities, several samples of normal urine were mixed with grape-sugar solutions, and the following experiments were then made:

"1. May 29th, 1886: A, normal urine, acid, 1.021; B, normal urine, acid, plus one-half per cent of sugar; C, normal urine, acid, plus one-fourth per cent of sugar; D, normal urine, acid, plus one-fourth per cent of sugar. May 30th, 1886: A, a small bubble on the top of the cylinder; B, $= 2\frac{2}{5}$ c.c. gas; C, $= \frac{2}{5}$ c.c. gas; D, $= \frac{3}{5}$ c.c. gas.

"2. May 31st, 1886: A, normal urine, acid, 1.020; B, normal urine, acid, plus one per cent of sugar; C, normal urine, acid, plus one-half per cent of sugar; D, normal urine, acid, plus one-half per cent of sugar; E, normal urine, acid, plus one-fourth per cent of sugar. June 1st, 1886: A, a small bubble on the top of the cylinder; B, $= 5\frac{2}{5}$ c.c. gas; C, $= 2\frac{2}{5}$ c.c. gas; D, $= 2$ c.c. gas; E, $= \frac{2}{5}$ c.c. gas; F, $= \frac{4}{5}$ c.c. gas.

"3. June 1st, 1886: A, normal urine, acid, 1.022; B, normal urine,

acid, plus one per cent of sugar; C, normal urine, acid, plus three-fourths per cent of sugar; D, normal urine, acid, plus one-half per cent of sugar. June 2d, 1886: A, a small bubble on the top of the cylinder: B, $= 5\frac{2}{3}$ c.c. gas; C, $= 3\frac{2}{3}$ c.c. gas; D, $= 2\frac{2}{3}$ c.c. gas.

"4. June 2d, 1886: A, normal urine, acid, 1.006; B, normal urine, acid, plus one per cent of sugar; C, normal urine, acid, plus one-half per cent of sugar; D, normal urine, acid, plus one-fourth per cent of sugar. June 3d, 1886: A, a small bubble on the top of the cylinder: B, $= 5\frac{2}{3}$ c.c. gas; C, $= 2\frac{2}{3}$ c.c. gas; D, $= \frac{2}{3}$ c.c. gas.

"5. June 24th, 1886: A, normal urine, acid, 1.024; B, normal urine, acid, plus one per cent of sugar; C, normal urine, acid, plus three-fourths per cent of sugar; D, normal urine, acid, plus one-half per cent of sugar; E, normal urine, acid, plus one-fourth per cent of sugar; F, normal urine, acid, plus one-eighth per cent of sugar. June 25th, 1886: A, a small bubble $= 0$; B, $= 5$ c.c. gas; C, $= 4$ c.c. gas; D, $= 2\frac{1}{2}$ c.c. gas; E, $= \frac{2}{3}$ c.c. gas; F, $= \frac{1}{10}$ c.c. gas.

"6. October 21st, 1886: A, normal urine, acid, 1.018; B, normal urine, acid, plus one-half per cent of sugar; C, normal urine, acid, plus three-fourths per cent of sugar. October 22d, 1886: A, a small bubble on the top; B, $= 2\frac{1}{2}$ c.c. gas; C, $= 3\frac{3}{5}$ c.c. gas.

"7. October 23d, 1886: A, normal urine, acid, 1.020; B, normal urine, acid, plus one-half per cent of sugar; C, normal urine, acid, plus three-fourths per cent of sugar; D, normal urine, acid, plus one per cent of sugar. October 24th, 1886: A, a small bubble on the top of the cylinder; B, $= 2\frac{1}{2}$ c.c. gas; C, $= 3\frac{2}{5}$ c.c. gas; D, $= 4\frac{2}{5}$ c.c. gas.

"8. October 26th, 1886: A, normal urine, acid, 1.020; B, normal urine, acid, plus one-fourth per cent of sugar; C, normal urine, acid, plus one-half per cent of sugar; D, normal urine, acid, plus three-fourths per cent of sugar. October 27th, 1886: A, a small bubble on the top; B, $= \frac{3}{10}$ c.c. gas; C, $= 1\frac{9}{10}$ c.c. gas; D, $= 3\frac{2}{5}$ c.c. gas.

"9. November 1st, 1886: A, normal urine, acid, 1.022; B, normal urine, acid, plus one-fourth per cent of sugar; C, normal urine, acid, plus one-half per cent of sugar; D, normal urine, acid, plus three-fourths per cent of sugar; E, normal urine, acid, plus three-fourths per cent of sugar; F, normal urine, acid, plus one per cent of sugar. November 2d, 1886: A, a bubble on the top $= 0$; B, $= \frac{1}{2}$ c.c. gas; C, $= 1\frac{3}{5}$ c.c. gas; D, $= 3\frac{1}{5}$ c.c. gas; E, $= 3\frac{3}{5}$ c.c. gas; F, $= 5$ c.c. gas.

"10. November 2d, 1886: A, normal urine, acid, 1.018; B, normal urine, acid, plus one-fourth per cent of sugar; C, normal urine, acid, plus one-half per cent of sugar; D, normal urine, acid, plus one-half per cent of sugar; E, normal urine, acid, plus three-fourths per cent of sugar; F, normal urine, acid, plus one per cent of sugar.

November 3d, 1886: A, a small bubble on the top; B, $= \frac{1}{5}$ c.c. gas; C, $= 2\frac{1}{5}$ c.c. gas; D, $= 2$ c.c. gas; E, $= 3\frac{2}{5}$ c.c. gas; F, $= 4\frac{2}{5}$ c.c. gas.

"If we take the numbers found in every experiment, then we have:

"For one per cent of sugar the gas volume equals $5\frac{2}{5}$, $5\frac{2}{5}$, $5\frac{2}{5}$, 5, $4\frac{2}{5}$, 5, $4\frac{3}{5}$ c.c.

"For three-fourths per cent of sugar the gas volume equals $3\frac{2}{5}$, 4, $3\frac{3}{5}$, $3\frac{2}{5}$, $3\frac{2}{5}$, $3\frac{3}{5}$, $3\frac{3}{5}$ c.c.

"For one-half per cent of sugar the gas volume equals $2\frac{2}{5}$, $2\frac{2}{5}$, 2, $2\frac{2}{5}$, $2\frac{1}{5}$, $2\frac{1}{5}$, $2\frac{1}{5}$, $1\frac{9}{10}$, $1\frac{3}{5}$, $2\frac{1}{5}$, 2 c.c.

"For one-fourth per cent of sugar the gas volume equals $\frac{2}{5}$, $\frac{3}{5}$, $\frac{2}{5}$, $\frac{4}{5}$, $\frac{2}{5}$, $\frac{2}{5}$, $\frac{3}{10}$, $\frac{1}{5}$, $\frac{1}{5}$ c.c.

"For one-eighth per cent of sugar the gas volume equals $\frac{1}{10}$ c.c.

"By this table it becomes evident that the numbers for the quantity of the gas volume in different samples of urine containing the same percentages of sugar are always approximately equal, and differ at the most by three-fifths cubic centimetres.

"The average numbers quoted in the table are: One per cent of sugar equals 5 c.c. gas; three-fourths per cent of sugar equals $3\frac{2}{5}$ c.c. gas; one-half per cent of sugar equals 2 c.c. gas; one-fourth per cent of sugar equals $\frac{2}{5}$ c.c. gas; one-eighth per cent of sugar equals $\frac{1}{10}$ c.c. gas.

"I intentionally avoided ascertaining the quantity of the gas volumes in smaller proportions than in quarters (one, three-fourths, one-half, one-fourth), in order that the differences of the gas volumes might be as great as possible, and that they could be easily distinguished from each other.

"With one per cent of sugar the gas volume is 5 c.c.; thus the gas fills nearly the whole cylindrical part of the fermentation-tube. If the urine contain a little more than one per cent of sugar, then the whole cylinder will be occupied by gas; the urine, pressed into the cylinder, will deliver all its carbonic acid into the air, and will give us in this way no means of ascertaining how much more than one per cent of sugar it has contained. Therefore, if a sample of urine is given to us for examination, and we make the fermentation test in the *graduated* fermentation-tube, we shall be able to say on the following day, *i. e.*, after the fermentation has taken place, whether the urine contains sugar or not, and if sugar, then how much of it, whether one eighth, one-fourth, one-half, three-fourths, one per cent, or more than one per cent; but we shall not be able to say by the first test alone how much more than one per cent of sugar the urine may contain.

"In order to ascertain by this fermentation test approximately the

quantity of sugar in urine containing more than one per cent of sugar, it is necessary to dilute it with water.

"Diabetic urine of a straw color, and with a specific gravity of 1.018 to 1.022, was usually diluted by me two times; of 1.022 to 1.028, five times; 1.028 to 1.038, ten times. The test is to be made with the diluted urine. After the reaction has been completed, the gas volume of the fermentation-tube is read, and thus the quantity of sugar ascertained; in this way the original (not diluted) urine will contain, in proportion to the amount of dilution, two, five, or ten times more sugar than the diluted one.

"As an example for the quantitative fermentation test, the following experiment may be mentioned:

"June 28th, 1886: A, diabetic urine, 1.040, diluted ten times; B, diabetic urine, 1.038, diluted ten times; C, diabetic urine, 1.020, diluted two times; D, normal urine, 1.010. June 29th, 1886: A, $= 3\frac{1}{5}$ c.c.; B, $= 2\frac{1}{5}$ c.c.; C, $= 5$ c.c. gas; D, a small bubble on the top of the cylinder. Thus A has $3\frac{1}{5}$ c.c. gas $= \frac{3}{4}$ per cent of sugar, the urine has been diluted ten times, therefore the original urine contains $7\frac{1}{2}$ per cent of sugar; B, $= 2\frac{1}{5}$ c.c. $= \frac{1}{2}$ per cent $\times 10 = 5$ per cent of sugar; C, $= 5$ c.c. $= 1$ per cent $\times 2 = 2$ per cent of sugar; D, no sugar.

"This method of ascertaining the quantity of sugar by fermentation I applied during several months in the examination of the urine of the diabetic patients of the German Hospital, and I was fully satisfied with the result. I also compared several times the results found by fermentation with the numbers given by the quantitative Fehling's solution test. As bearing on this point, the following two experiments may be mentioned:

"1. *Fermentation test.*—June 10th, 1886: A, diabetic urine, 1.040, diluted ten times; B, diabetic urine, 1.026, diluted five times; C, diabetic urine, 1.020, diluted five times; D, normal urine. June 11th, 1886: A, $= 4\frac{1}{5}$ c.c. gas $=$ over $\frac{3}{4}$ per cent $\times 10 =$ more than $7\frac{1}{2}$ per cent of sugar; B, $= 2$ c.c. gas $= \frac{1}{2}$ per cent $\times 5 = 2\frac{1}{2}$ per cent of sugar; C, $= 1$ c.c. gas $=$ over $\frac{1}{4}$ per cent $\times 5 =$ more than $1\frac{1}{4}$ per cent of sugar; D, no sugar.

"*Fehling's test.*—A. $= 7\frac{1}{2}$ per cent; B, $= 2$ per cent; C, $= 2$ per cent of sugar; D, no sugar.

"2. *Fermentation test.*—June 14th, 1886: A, diabetic urine, 1.032, diluted ten times; B, diabetic urine, 1.035, diluted ten times; C, diabetic urine, 1.024, diluted five times; D, normal urine. June 15th, 1886: A, $= 2\frac{2}{5}$ c.c. gas $= \frac{1}{2}$ per cent $\times 10 = 5$ per cent of sugar; B, $= 3\frac{3}{5}$ c.c. gas $= \frac{3}{4}$ per cent $\times 10 = 7\frac{1}{2}$ per cent of sugar; C, $= \frac{3}{5}$ c.c. gas $= \frac{1}{4}$ per cent $\times 5 = 1\frac{1}{4}$ per cent of sugar; D, no sugar.

"*Fehling's Test.*—A,=5 per cent; B,=6½ per cent; C,=1⅔ per cent of sugar; D, no sugar.

"If we now compare the results of the quantitative test by Fehling's solution with the results found by the fermentation test, we find that they are not always absolutely equal, although the difference is but slight. In this way it appears that the method of ascertaining the quantity of sugar by the gas volume in the fermentation tube gives true and approximately correct results.

"The advantages of this mode of ascertaining the quantity of sugar consist in its being neither troublesome nor complicated, and it can also be employed by every physician. Urine containing albumin can be *directly* examined for sugar by the fermentation test; 'it is not necessary to separate the albumin before applying the test, as in other methods.' That is another point in favor of the fermentation test.

"In order to make the quantitative determination of sugar yet easier, we have written on the cylinder figures showing the percentages of sugar. A fermentation-tube bearing this scale shows directly, by the level of the urine, the per cent of sugar, and can be therefore called 'Fermentation Saccharometer.'

FIG. 53.—FERMENTATION SACCHARO-
METER.

"From a study of the experiments detailed in this article we may formulate the following conclusions:

"*First.*—The fermentation test can be made in the ordinary temperature of the room.

"*Second.*—The addition of mercury is not necessary.

"*Third.*—The volume of developed gas in the cylinder gives us an idea of the approximate quantity of the sugar present in the urine."
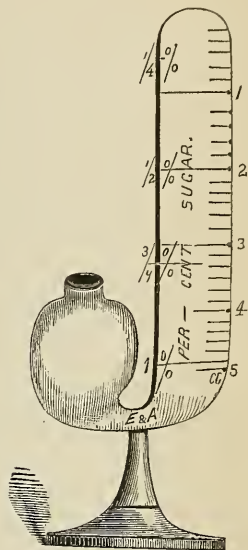
CHAPTER V.

NITROGENOUS EXCRETORY SUBSTANCES.

There are a number of groups of nitrogenous substances which represent the physiological metamorphotic transformations of the body, some of which appear normally in the urine, and are the complete products of tissue waste. But the larger number are found in the blood or the various organs and fluids which constitute the animal organism. Some of them appear constantly in the urine, but in such small quantities that they are not easily recognized, and consequently afford no practical information; others appear as abnormal constituents, and for the same reasons are equally unimportant. Still the time may not be far distant when each of these complex substances may be more easily recognized and, when occurring in the urine, they will be found to be indicators of diseased conditions; their presence or absence enabling the physician to attain greater skill in diagnosis.

They are given in tabular form to show their great variety, and as indicative of the manifold number of products which may be formed when their normal development is interrupted. It also suggests a variety of these incomplete products as the cause of the great diversity of symptoms classed under the general term uræmia or uræmic poisoning.

1. Urea, CH_4N_2O, or $(NH_2)_2$ CO
2. Uric Acid, $C_5H_4N_4O_3$
3. Kreatin, $C_4H_9N_3O_2$
4. Kreatinin, $C_4H_7N_3O$
5. Allantoin, $C_4H_6N_4O_3$
6. Sarkosin, $C_3H_7NO_2$
7. Hypoxanthin, $C_5H_4N_4O$
8. Xanthin, $C_5H_4N_4O_2$
9. Carnin, $C_7H_8N_4O_3$
10. Guanin, $C_5H_5N_5O$
11. Kynurenic Acid, $C_{20}H_{14}N_2O_6$ + + $2H_2O = C_{20}H_{18}N_2O_4$
12. Glycin, $C_2H_2(NH_2)O(OH)C_2H_5-N_3O_2$
13. Taurin, $C_2H_7NO_3S$
14. Leucin, $C_6H_{13}NO_2$
15. Cystin, $C_3H_7NSO_2$
16. Benzoic Acid, $HC_7H_5O_2$
17. Tyrosin, $C_9H_{11}NO_3$
18. Hippuric Acid, $C_9H_9NO_3$
19. Phenylic Acid, C_6H_6O
20. Glycocholic Acid, $C_{26}H_{43}NO_6$
21. Taurocholic Acid, $C_{26}H_{45}NSO_7$
22. Indican, $KC_8H_6NSO_4$
23. Indigo, $C_8H_5N_9O$
24. Indol, C_8H_7N
25. Skatol, C_9H_9N
26. Inosite, $C_6H_{12}O_6$
27. Cerebrine, $C_{17}H_{33}NO_3$
28. Lecithine, $C_{42}H_{84}NPO$
29. Neurine, $C_5H_{13}N$

UREA (CH_4N_2O).

Next to water, urea is the most abundant and important normal ingredient found in urine. It constitutes nearly one-half of the solid constituents. The average amount of urea excreted daily is estimated by physiologists at about 550 grains (35.637 grams). Admitting the daily average of urine voided to be 50 ounces (1555.170 c.c.), and the above figure the quantity of urea excreted, the percentage of urea eliminated will be 2.2 per cent per diem. All these figures are liable to very wide variations from day to day, and from hour to hour, in a state of perfect health and, of course, to a still greater extent in disease.

The kind and quality of food, the quantity of fluid taken, the amount of exercise, and the hour of the voiding of the urine, all have their influence in determining the quantity of urea to be formed and excreted. The activity of the integumental and alimentary excretion also must not be overlooked.

Remembering all these *facts*, and especially those relating to diet and exercise, the absolute daily quantity of urine excreted must be ascertained, and the test made from the mixed sample to obtain anything like trustworthy information. The examination of the urine for one day will be of no service, but it must be repeated for several days in succession, and these results must be added together and divided by the number of examinations and days to yield anything like approximate accuracy.

With all this, the quantitative test must be accurate and the calculations carefully computed, otherwise the greatest error will be the result.

Unless every article of diet was carefully analyzed, in conjunction with the greatest possible accuracy in quantitative analysis of urine, no positive information could be obtained, and even then a highly nitrogenous meal might slip through the alimentary tract undigested and unabsorbed.

When all these possible chances for error are considered in ascertaining the precise quantity of urea eliminated and its relation to the amount of urea-forming elements imbibed, and the variously interrupted metabolic transformations, the practical importance of estimating the precise quantity of urea eliminated is reduced to the minimum, if not absolutely lost, in reference to any information regarding diseased processes.

The exact amount of urea excreted may be determined, but it furnishes no information as to the source and cause of the non-elimina-

tion. It simply assures the examiner that the diminution in specific gravity is due to a deficient elimination of urea, and as this is about the only cause for a diminished density, we can in all cases assume it to be due to this. The knowledge that the loss of urea is three-tenths or five-tenths of one per cent is of no practical value. It neither aids in diagnosis, prognosis, nor treatment.

There are a number of methods for the quantitative analysis of urea. Most of them, however, have certain objections and uncertainties, which, with the above reasons, renders them very troublesome and almost useless. A few of them, however, will be given. Among these may be mentioned the methods of Russell and West, Liebig, Davy, Fowler, Squibb, and Doremus.

The test of Russell and West is one of the most accurate in use. There are, however, some serious objections to it. The outfit is somewhat expensive and easily broken. It is difficult to manipulate unless the examiner is accustomed to such work. There is also danger from inhaling the fumes of the bromine, and the laboratory, office, or house may become filled with its pungent odor.

The apparatus which has been in use at the laboratory of the New York Post-Graduate Medical School and Hospital consists of graduated pipettes, and a registered collecting and a generating bulb tube, the one to hold the solutions and the other to collect the gas set free; a pneumatic trough on long legs, with a perforated stopper, arranged to receive the generating tube below and the collecting tube above.

The directions for using are: Fill the small pipette up to the neck with the sample to be tested; this will measure exactly five cubic centimetres (77.161 minims); let it flow down the bulb, then pour in water until it rises to the top of the constriction. The amount of water to be added to reach this point is fifteen cubic centimetres (231.485 minims).

Put in the long stopper, and see that no air is below it.

Fill the measuring tube, and invert it in the trough, which has previously been filled with water, and drop it into the socket to steady it until the generating tube has been attached. Fill up the bulb tube with the hypobromate solution. The amount required for the test is 28 cubic centimetres. This, however, does not always fill the tube, and water has to be added to displace all the air.

Pull the long stopper over the perforated cork, insert the bulb tube from below, and slip the measuring tube into the socket over the perforated cork and bulb tube as quickly as possible to prevent the loss of any of the gas.

Warm the bulb until it feels quite hot, or keep it in a sufficiently warm place.

If the five cubic centimetres of urine give off more nitrogen gas than the measuring tube will hold, dilute the urine with an equal volume of water, and take five cubic centimetres of the dilution, read off the result on the measuring tube, and multiply by two. It is always best to dilute the urine.

If the urine contains albumin, heat to boiling with two or three minims of acetic acid, filter, and take five cubic centimetres of the filtrate.

The figures 1, 2, and 3 marked on the measuring tube are to be read 1, 2, or 3 grams of urea for each 100 cubic centimetres.

The hypobromite solution is prepared by first making a caustic soda solution, and then adding the bromine.

To make the soda solutions, 100 grams of pure caustic soda are dissolved in 250 cubic centimetres of distilled water and filtered. When cold, the addition of 25 cubic centimetres of bromine completes the hypobromite solution. As this keeps badly, it is better to make the soda solution, which keeps well in large quantities, and only add the bromine at the time of using.

To make just the required 28 cubic centimetres, take 22.4 cubic centimetres of the caustic soda solution, and add 5.6 cubic centimetres of bromine. But owing to the danger in measuring the bromine, it is much better to take the whole bottle which holds 10 cubic centimetres, and add 40 cubic centimetres of the soda solution. From this mixture the required 28 cubic centimetres can easily be measured and transferred to the bulb tube with safety to the manipulator.

The bromine should be opened and added to the soda solution in the open air, with the back to the wind.

It takes an ordinary one-ounce vial of bromine, price 35 cents, to make 10 cubic centimetres.

The conversion of the metric system is made by considering one gram or cubic centimetre equal to 15.43234874, and allowing 480 grains or minims to the ounce.

1. gram,	. .	= 15.4323 +	minims.
2. "	. .	= 30.8646 +	"
3. "	. .	= 46.2970 +	"
5. cubic centimetres	= 77.1617 +	"
5.6 " "	= 86.4211 +	"
10. " "	= 154.3234 +	"
15. " "	= 231.4852 +	"

17

22.4 cubic centimetres	=	345.6846 +	minims.
25. " "	=	385.8087 +	"
28. " "	=	432.1057 +	"
40. " "	=	1.2860 +	ounces.
100. grams, . .	=	3.2850 +	"
250. cubic centimetres	=	8.0376 +	"

The above-described apparatus is the one which has been used for several years past, both in experiments and for testing urine. It has been greatly modified and made quite simple by Opjohn.

Davy's, like the Russel and West method, is based upon the splitting up of the urea into nitrogen, carbon dioxide (CO_2), and water. In the Russel and West test, the carbon dioxide (CO_2) is absorbed by the caustic alkali or hypobromite solution; in Davey's, by the hypochlorate solution.

Liebig's is still more complicated, but by it [or that of Davy in the hands of an expert chemist, very accurate results can be obtained. But in both there are so many chances for error and so many corrections to be made, that, practically speaking, for every-day office work they are not to be recommended.

The test introduced by Dr. G. B. Fowler, of New York City, is easily manipulated and is quite practical. All the appliances needed are a long glass cylinder capable of holding 10 or 12 ounces (311.034 c.c. or 373.242 c.c.), and graduated in ounces and fractions; two large and accurate urinometers, one registering densities from 1.000 to 1.030, and the other from 1.030 to 1.060. The whole cost being about five dollars.

The principle of the test consists in the liberation of the nitrogen gas and the carbon dioxide (CO_2), by the action of the liquor sodæ chlorinatis or Labarraque's solution.

The test is used as follows: Take seven ounces (217.314 c.c.) of the chlorinated soda solution of a *known* density of 1.045, and multiply it by seven, add one ounce (31.103 c.c.) of urine having a specific gravity, say of 1.010. As the evolution is so sudden, the specific gravity of the combined fluids has to be accounted for before uniting. Take 7 ounces of the soda solution at $1.045 \times 7 = 7.315$, add to this the one ounce (31.103 c.c.) of urine with a density of 1.010 and divide by eight, and it will give $1.040\frac{3}{8}$ as the specific gravity of the combined fluids, viz., $1.045 \times 7 = 7.315 + 1.010 = 8.325 \div 8 = 1.040\frac{3}{8}$. At the end of an hour or more, the density will have fallen; if to 1.039, it indicates a loss of $1\frac{3}{8}$ degrees in density. By multiplying this loss by the factor 7.791, it will indicate the number of milligrams of urea lost in every 100 cubic centimetres of urine, or, if we multiply

the loss by the factor .77, it will give the amount lost in percentage; in this example it would indicate a loss of 14.65 milligrams in every cubic centimetre, or 1.46 per cent.

FIG. 54.
GLASS CYLINDER GRADUATED IN OUNCES OR CUBIC CENTIMETRES.
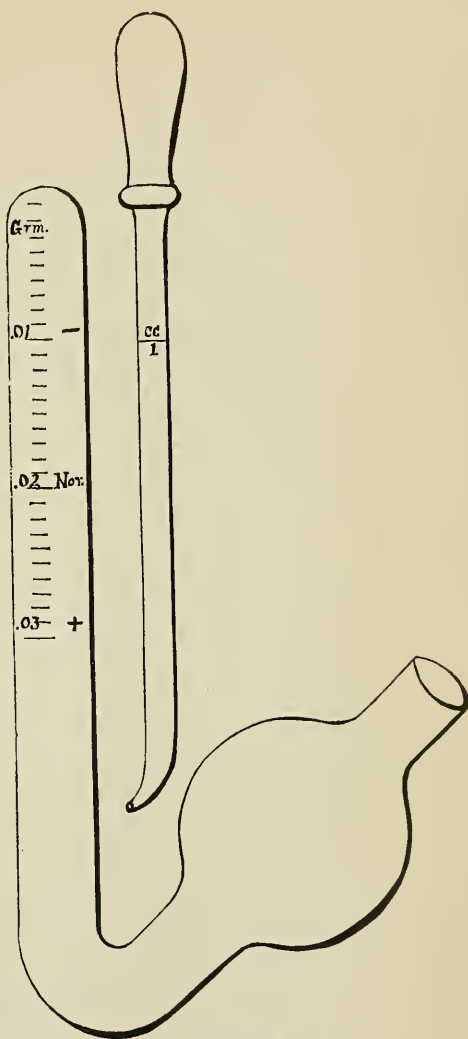
FIG. 55.
UROMETER OF DOREMUS, REDUCED ABOUT ONE-THIRD.

The following method, as given by Dr. Charles A. Doremus,[1] of this City, is the most practical of all.

[1] New York Medical Record, March 14th, 1885, p. 302.

"The form of apparatus shown in the figure has been found to yield results so closely in accord with theory that its employment for rapid clinical examination of the urine may lead to a more frequent analysis for urea on the part of the physician and be the means of securing data concerning the elimination of so important an excrementitious substance which will be beneficial.

"The manipulation of the urometer is simple in the extreme. By inclining it, the long arm may be filled with the hypobromite to the bend at the bulb. By means of the nipple pipette, a measured volume of the urine (1 c.c.) is injected slowly up the long arm by compressing the nipple. A rapid decomposition of the urea takes place, the bubbles of nitrogen rising in the long arm, while the displaced liquid flows into the bulb, which serves as a reservoir. With a little care the urine may be delivered at a rate that permits the decomposition to take place without loss of gas. The graduation on the glass indicates the weight of urea in the urine used.

"Two forms of apparatus are made, one graduated to read fractions of a gram (0.00 to 0.03 per 1 c.c. of urine), the other to show grains of urea in the fluidounce of urine. When the volume passed in twenty-four hours is known, the calculation of the analysis is very easy. Total quantity of urine voided, 1.600 c.c.; urea in 1 c.c. of urine (result of analysis) 0.024 grams; urea in 1.600 c.c = 0.024×1.600 c.c. = 38.4 grams. When the centesimal graduation is used, the weight of urea in 100 volumes of urine is ascertained by multiplying the result of the test by 100. This gives what is commonly termed the percentage of urea. This is not strictly correct, but the true percentage can be calculated when the specific gravity of the urine is taken thus: specific gravity of urine, 1.020; urea in 1 c.c. of urine, 0.02 grams; 100 c.c. of urine would weigh 102 grams if the specific gravity was 1.020, therefore,

$$102 : 100 :: 2 : x = 196, \text{ the true percentage.}$$

"When the tube graduated in grains is used, the calculation of the percentage is a more complicated arithmetical problem. The ounce contains 455.7 grains. From this, the specific gravity, and the result of the analysis the computation can be made.

"The hypobromite solution is prepared according to the formula of Knop, by dissolving 100 grams of sodium hydrate in a 250 c.c. of water. This solution may be kept in a bottle with a paraffined stopper. Bromine is mixed with this in the proportion of one volume to ten; 2 c.c. of bromine with 20 of the sodium hydrate will suffice for two tests. After the bromine has united with the alkali, the liquor is diluted with its own volume of water.

"When using English weights, six ounces of sodium hydrate are dissolved in a pint of water to make the alkali. The bromine should be added to this in the proportion of one to ten, and the liquid diluted with its own volume of water. A fresh, good, hypochlorite will serve for the hypobromite when the latter cannot be obtained.

"The normal quantity of urea voided is two per cent or .02 grams per c.c. or 10 grains per ounce. The elimination of a diminished or increased quantity of urea is speedily determined by the use of the apparatus.

"Messrs. Eimer & Amend supply either form at a very moderate price."

As already explained, there is no very practical information to be obtained from such analyses, on account of the numerous sources of error and the many daily variations independent of disease.

Further than this, the non-elimination of urea does not indicate its accumulation in the blood, and even if it did, it proves nothing, for experimentally it has been proven that hypodermic injections of urea produce none of the effects commonly witnessed in so-called uræmic attacks, but large doses are more likely to produce the opposite or a soothing influence upon the nervous system.

There is not the slightest doubt that incomplete physiological metamorphosis is the cause of the so-called uræmic manifestations. But just what the irritating and poisonous substance is has not as yet been clearly elucidated.

Taking all these things into consideration, it appears that very little, if any, additional information is obtained by knowing the precise number of grains or the percentage of urea lost. The loss of density in connection with the quantity, as indicated by the urinometer affords equally as much information.

Clinical Significance of Urea.—Urea naturally is more abundant in the urine of children than in that of adults, which is explained by the greater amount of muscular activity and the growth and development requiring more nitrogenous food.

Urea is also increased during the period of rest following muscular activity in the adult.

Urea is increased in quantity during the early activity of all acute and febrile diseases. The only recorded exception to this is Frerichs' case of acute atrophy of the liver, in which he found the urine deprived of urea. In other cases, he found it increased.

As these acute diseases advance and the renal cells undergo progressive metamorphotic changes and lose their eliminating power, the quantity of urea is diminished. This non-formation and elim-

ination of urea with the retention of incomplete products in the
circulating blood appears to be the great cause for the increased
bodily temperature, and is the principal factor in exciting and main-
taining the cerebral manifestations. If, for any reason, the incom-
plete products accumulate very rapidly, they almost completely over-
throw the nervous centres, and a fall in or a low bodily temperature
is the result. It is a firm conviction based upon an extended necropsy
study that in all the acute diseases the height of the attack and the
prognosis rests almost exclusively upon the minute changes in the
hepatic and renal epithelial cells. When this fact is more generally
accepted and acted upon, the mortality in connection with all acute
and severe diseases and after severe surgical operations will be
diminished, other things being equal. The greatest antipyretic will
be that drug or that plan of treatment which will prevent the retro-
grade metamorphosis of the hepatic and renal epithelial cells and sus-
tain their nutrition and eliminative activity.

During the defervescence of these diseases, there is a state of phy-
siological inactivity and the urine contains but very little urea. From
this time on, however, the urea in the urine will steadily increase in
quantity, in direct proportion to the return of the functional activity
of the epithelial corpuscles of the kidneys, until the normal standard
has again been attained.

If there has been a permanent impairment, it is apt to remain below
normal.

It is a well-known clinical fact that in all forms of renal lesions
there is a diminution in the quantity of urea excreted, but this is not
the case in connection with the chronic diseases implicating the other
visceral organs. Peculiar nervous manifestations are the rule with
the renal lesions and the exception with the other chronic diseases.

With glycosuria the urea is increased in the urine up to the time
that the renal cells fail, and then a decrease in the quantity of urea
eliminated is noticed, followed by marked nervous symptoms, uræmia,
and death.

From these clinical and pathological observations, this assumption
is justified, that the function of the renal epithelial cells is to pick up
from the blood the urea-forming elements, convert them into com-
pletely formed urea, and discharge them into the lumen of the urinif-
erous tubules.

If the urea accumulated in the blood was in direct proportion to its
disappearance in the urine, this theory would not be sustained, but
since this is not the case, it would appear to more fully substantiate
the idea here advanced. The elimination of large quantities of water,

which is principally discharged through the Malpighian tufts, and but slightly, if at all, through the epithelial cells, increases the quantity of urea excreted, and consequently its action in regard to this agent must be purely mechanical. Passing over the excretory cells in large quantities, it keeps the free surface clean and possibly by a suction force helps to draw the solid particles from the protoplasm or through the rods of Heidenhain. Therefore, the quantity of urea eliminated is one of the great indicators by which we are enabled to judge of the extent and degree of retrograde metamorphosis going on in the renal epithelial corpuscles. But a careful microscopic study of the epithelium of the casts will give more accurate information in regard to the condition of the kidneys.

URIC ACID ($C_5H_4N_4O_3$).

It is well known that uric acid is one of the products resulting from proteid metabolism, but as to the exact point of its formation, there is considerable doubt. It is a normal ingredient of the urine and is apparently a less complete product of tissue waste than urea. By some it is thought to be antecedent to the formation of urea. It has been found in the blood, liver, and spleen, and it has been claimed that it was more abundant in the spleen than at any other portion of the body. But about an equal quantity is found in the portal and hepatic blood. From this abundance in the spleen an abnormal quantity in the urine has been attributed to a faulty action on the part of that organ, but its presence in the urine after the removal of the spleen upsets this argument.

The views already advanced in relation to the acidity of the urine and the formation of urea and our clinical data point towards a similar method of formation for uric acid and traces its origin to the liver.

The chemico-physiological action of the liver is to develop the uric-acid-forming elements which are taken up from the blood, and are finally discharged into the uriniferous tubules as completely formed uric acid. This is borne out by our clinical data, for in all cases in which uric acid is abundant, the functions of the liver appear to be incompletely performed and there is also a hypertrophic condition of the renal cells. A typical pathological example of this is to be found in diabetes, in which primary changes in the liver are followed by an hypertrophic swelling of the epithelial cells, and finally their total destruction. Here an abundance of uric acid in the urine is not infrequent. The lack of an abundance of this acid in primary lesions

of the kidneys also points towards the renal cells as the final seat of production.

The finding of the small crystals of uric acid in the renal epithelial cells, when sections are made from these organs, is also proof of their formation at this point.

Uric acid requires from ten to fifteen thousand parts of water to hold it in solution. It is also less soluble in acid than alkaline solutions. On account of this great insolubility, and its liability to be deposited in the renal organs, and the frequency of its occurrence, it becomes one of the excreta which is most likely to induce a permanent renal lesion. This condition has been considered the principal excitant of Bright's.

Careful clinical observation demonstrates that this condition cannot be directly traced to any special kind of food. It is quite as likely to appear with vegetable as animal diet. That it has its origin in the nitrogenous compounds is, however, quite certain. The explanation of its occurrence upon a vegetable diet appears to be this. The carbonaceous substances are more easily transformed than the nitrogenous; over-indulgence in the former, therefore, exhausts the hepatic transforming power, so that the nitrogenous elements are only incompletely acted upon, the quality of bile becomes impaired, and finally uric acid is found in abundance in the urine. The return to a well-selected mixed diet will often obviate the difficulty; in other cases, a small allowance of purely albuminous diet is followed by good results, but in the larger proportion of cases the deficiency in the quality of the bile must be compensated for before anything like a permanent cure can be effected.

In some instances the appearance of uric acid in the urine may be due to an incomplete oxidation into complete urea, but in the larger number the cause is farther back and due to the incomplete hepatic metabolism.

The question of a uric acid *diathesis* is often raised. It would appear from the above that there is no condition truly deserving of the title uric or uric acid diathesis. The symptom accredited to such a condition is its appearance in the urine in abundance; the cause is an interruption in the physiological functions in the liver and the kidneys. It frequently occurs in families in which the methods of living are such that the liver is constantly overworked and incompletely supplied with oxygen. The children and grandchildren live as their forefathers have done, and consequently suffer in like manner. A change of habit, however, will cause a disappearance of the symptoms, which argues strongly against a diathesis.

The crystals of uric acid may accumulate in the pelves of the kidneys, forming what is commonly known as a renal calculus, their discharge giving rise to severe and sometimes dangerous symptoms, known as renal or nephritic colic. After their escape from the ureters, they may lodge in the bladder and form the nucleus for a uric acid or even a phosphatic calculus, or, in fact, any form of cystic stone; or they may be discharged with the urine, causing painful micturition or "scalding."

When abundant, they are plainly visible to the unaided eye.

The qualitative test for determining the presence of this acid is known as the *murexide reaction,* and is employed as follows:

Place a small quantity of the reddish crystalline deposit or some of the crystals in a watch-glass or on a glass slide; add four or five drops of nitric acid, and heat very cautiously over a spirit lamp or Bunsen's burner. The uric acid will dissolve, and a reddish-yellow residue will be obtained. Ammonia vapor or a small drop of ammonia added to the residue will produce a beautiful purplish-red color; on the subsequent addition of a little solution of caustic potash, it will assume a violet tint.

It has also been found that uric acid has the property of reducing copper in a similar manner to sugar (Pavey and Satterthwaite). It, however, requires longer boiling, and the copper test should be employed in the following proportions:

Take one drachm (3.887 c.c.) of the urine, add twenty (1.295 c.c.) minims of a twelve-per-cent solution of sulphate of copper, then add two and one-half (9.719 c.c.) of liquor potassæ, and boil. At the end of ten minutes' steady boiling, if uric acid be present, the reduction will be effected and a reddish deposit will be produced, which, after standing for a little while, is as positive as that of glucose.

The quantity can be determined in two ways; first, by precipitating with hydrochloric acid and collecting the crystalline deposit upon a weighed filter; and second, by the method suggested by Dr. Pavey. This also consists in the reducing power of uric acid on cupric sulphate.

Both methods, however, are too complicated to be of any practical value to the general practitioner, and a further description of them is omitted.

Diagnosis.—This is readily made when the crystals are found in the urine.

Prognosis.—Depends upon the treatment and the physician's success in regulating the patient's diet and habits.

Treatment.—If due to a deficient supply of oxygen, this should be

increased; in fact, in all these cases they should take pains to exercise freely in the open air. The next step is to regulate the diet, either placing them upon a limited mixed, or one which is exclusively nitrogenous. The main object is to improve the stomach and intestinal digestion, that absorption and further assimilation can be as easily effected as possible.

If there is reason to believe that the quantity and quality of bile are deficient, a little may be added in the way of fel bovis inspissatum, which in itself is often quite sufficient to remove the difficulty and cure the disease.

All forms of tonic cholagogues will be found of service.

Tonics only do good by improving the general condition of the digestive tract. If the abnormal condition is attributable to a depression of the nervous system, the nerve tonics should be used, and one of the best for its influence upon the nervous mechanism of the liver is damiana and its preparations, either alone or in combination. The dilute nitro-hydrochloric acid in ten-minim doses often proves itself of service as a tonic to the hepatic function: it, however, is more palliative than curative.

KREATIN $(C_4H_9N_3O_2)$.

This is one of the products of muscular metamorphosis, and probably never occurs in the urine under its own form. By losing one element of water, it is converted into kreatinin, which is one of the normal constituents of the urine. The finding of kreatin in a sample is generally believed to be due to the process of obstruction which causes an element of water to be joined to kreatinin.

KREATININ $(C_4H_7N_3O)$

is one of the complete products of tissue metamorphosis, and is always present in urine. The quantity eliminated daily is quite small, 15.432 grains (1 gram). It is one of the most powerful organic alkalies found in connection with the animal economy. Therefore, it is reasonable to suppose that the relative proportion existing between the formation and elimination of uric acid and kreatinin must largely govern the reaction of the urine. But on account of the small quantity and the difficulty of recognizing the presence of the latter, the examination for kreatinin in the urine has not yet been made practical.

ALANTOIN $(C_4H_6N_4O_3)$

is found in the alantoic fluid of the fœtus and in the urine of animals for a few days after birth, and may be found in the excreta in minute quantities later in life.

It is one of the products resulting from oxidization of uric acid, and ordinarily is further transformed and eliminated as urea.

It has been found in the human urine after taking tannic acid.

SARKOSIN $(C_5H_7NO_2)$

appears to be derived from kreatin, and only appears in the urine when large quantities have been ingested. Its presence prevents the precipitation of the urea by mercury, and consequently interferes, when present, with the quantitive estimation by this method.

HYPOXANTHIN $(C_5H_4N_4O)$

or sarkine is a normal constituent of muscles, and has been found in the spleen and medulla of the bones. It has been found in the blood and urine in connection with leucocythæmia. Bence-Jones also found it in the urine of a boy nine years old, as a crystalline deposit. Hypoxanthin crystals were found by Lebon in a vesical calculus.

XANTHIN $(C_5H_4N_4O_2)$.

Xanthin appears to be a higher oxide of the former. It was first discovered in a urinary calculus, but has since been recognized as a urinary crystalline deposit. It is very insoluble in water, requiring 1,500 times its bulk at 100° C. (180° F.).

The *clinical significance* of hypoxanthin and xanthin is chiefly in their insolubility, especially in the case of the latter, and consequently their tendency to form calculi.

CARNIN $(C_7H_8N_4O_3)$ AND GUANIN $(C_5H_5N_5O)$.

These two substances, up to the present time, have only been found in extracts from the tissues of the body, and have not been traced into the urine in their own form.

KYNURENIC ACID $(C_{20}H_{14}N_2O_6. + 2H_2O)$.

Kynurenic acid has, so far, only been found in the urine of dogs.

GLYCIN ($C_2H_2(NH_2)O(OH)$ $C_2H_5N_3O_2$).

Glycin has not been traced into the urine as a distinct element, but is one of the nitrogenous products which may be obtained by the decomposition of hippuric acid or bile acids.

TAURIN ($C_2H_7NO_3S$).

This is a constituent normal to the hepatic secretion, but occasionally passes out of the body in the urine. It is not easy to detect its presence, and is therefore of no practical value.

LEUCIN ($C_6H_{13}NO_3$).

This substance is occasionally found in the urine in an incomplete crystalline form, in connection with tyrosin. It has been found in connection with acute yellow atrophy of the liver, acute phosphorus poisoning, leucocythæmia, typhoid fever, small-pox, etc. Its *clinical significance* is the same as tyrosin.

Scherer's Test for Leucin.—If pure leucin is evaporated with nitric acid, a colorless, almost imperceptible residue remains. Add hydrate of soda, the leucin dissolves, and according to its purity forms a colorless, or more or less colored fluid. If it be collected upon a piece of platinum foil, it forms an oil-drop, which does not wet the platinum, but rolls about without adhering to it. This is also quite characteristic of very impure leucin.

CYSTIN ($C_3H_7NSO_2$).

This crystalline substance has been found in connection with urinary calculi, and also as a urinary sediment. But at present our knowledge of it is very meagre and its *clinical significance* very uncertain.

BENZOIC ACID ($HC_7H_5O_2$)

is one of the non-nitrogenous compounds resulting from a splitting up of hippuric acid, and is only found in the urine in connection with a decomposition of this acid, and after eating freely of asparagus.

TYROSIN ($C_9H_{11}NO_3$)

has been found in the urinary sediment as fine needle-like crystals collected into feathery masses. In alkaline solutions they often form rosettes, composed of the fine needles arranged radially. On boiling with Millon's reagent (see page 226), the fluid will become red.

Piria's Test for Tyrosin.—Gently warm with strong sulphuric acid, add chloride of iron, a violet color will be produced if the crystals are tyrosin.

It has, like leucin, been found in connection with acute yellow atrophy of the liver, acute poisoning by phosphorus, leucocythæmia, typhoid fever, small-pox, etc.

Clinical significance.—The appearance of leucin and tyrosin in the urine is unquestionably indicative of a very marked interruption in the metabolic processes of the body, and especially of the liver, and is evidence of the great severity of the primary disease.

HIPPURIC ACID $(C_9H_9NO_3)$.

This substance is found in abundance in the urine of herbivora, but in the human subject only 4.409 grains (0.35 grams) are excreted daily. It crystallizes in the shape of fine needles or four-sided prisms. It is soluble in 600 parts of cold water. Its quantity in the urine is increased by eating plums, red whortleberries, bellberries, mulberries, asparagus, and by taking benzoic acid, oil of bitter almonds, toluol, cinnamonic acid, kinnic acid, etc.

It has also been found in abundance in the acute fevers, diabetes, cholera, etc.

Clinical importance.—A vegetable diet appears to increase the formation of this acid. From this and the fact that benzoic acid or the benzoates have a tendency to increase this acid in the urine, it was at one time much lauded as a specific for the uric acid diathesis. It was, however, found of no special benefit, and if the reasons already advanced be true in relation to the formation of urea and uric acid, there is no physiological grounds for assuming that an increased formation of hippuric acid is going to produce a change in the metabolic action of the hepatic and renal cells in relation to the oxidation and formation of the uric acid.

The use of benzoic acid and its compounds may be of service in connection with alkaline urine, and has often been found a great aid in cystic inflammations.

PHENOLIC ACID (C_6H_6O).

This acid only occurs in the urine. At one time it was regarded as a normal constituent, but it is believed to be, more accurately speaking, a product of decomposition. After carbolic acid poisoning it has been found by several observers, while others have failed to detect its presence.

TAUROCHOLIC AND GLYCOCHOLIC ACIDS $(C_{26}H_{45}NSO_7)$
AND $(C_{26}H_{43}NO_6)$.]

These two are known by the common name of the biliary acids. They are proteid compounds which have their origin in the liver, and normally are poured into the alimentary tract with the bile. Here they aid in digestion, and are again reabsorbed and reconverted either by the hepatic cells or while in the blood. They may be found in connection with icterus or an over-production of bile, with all acute febrile diseases in which there is a marked blood poison, with acute poisoning by antimony, copper, phosphorus, and arsenic, and in acute yellow atrophy of the liver.

Their principal *clinical significance* is that they can be found in the urine a day or two in advance of the biliary pigments. They may even be found when no pigment escapes.

The test for the bile acids or salts is Pettenkofer's, which is employed as follows:

Prepare a standard solution of cane sugar of the strength of one part to four of distilled water. Add one minim (0.064 c.c.) of the saccharated solution for every ounce (31.103 c.c.) of the suspected sample, then a few minims of sulphuric acid; this will decompose the bile acids, and be followed by the formation of cholic acid. If the solution contain less than one five-hundredth of one per cent, no further change will occur; if, on the other hand, there is more than one five-hundredth of one per cent, the addition of a little more sulphuric acid will be followed, first by a cherry-red color, which soon changes to a deep violet.

The bile acids have to be first precipitated and isolated before this test can be applied, and for this reason it is not of practical value in connection with urinary analysis.

Strassburgh's modification is applied to the urine as follows: Dip a piece of filter paper into the fluid, and let it dry completely; put one drop (0.064 c.c.) of sulphuric acid on the dried filter paper, and let it run off; after a few seconds a deep violet color is developed, best seen by transmitted light.

This, unfortunately, like Pettenkofer's and all its modifications, is inaccurate and uncertain in urinary samples, and consequently devoid of practical value.

Both tests also give nearly the same reaction with solutions containing albuminates, amyl alcohol, ethereal oils, olein, oleic acid, and the salts of morphine and codeia. The only method of differentiation is a spectroscopic examination.

INDOL (C_8H_7N), INDICAN ($KC_8H_6NSO_4$), AND INDIGO ($C_8H_5N_2O$).

These three substances are closely allied to each other. They are supposed to originate as indol, which is developed by the liver, although pancreatic fermentation has also been considered as the place and means of its formation, while experimental investigation has led to the belief that it only develops in the latter organ when bacteria are present, and that its development is due to their action.

There is no doubt but that indol is present in the alimentary canal, and that some of it passes out with the fæces, and gives rise, in part at least, to their peculiar odor. The remaining portion is absorbed with the chyme, and appears in the urine as indican. Here it is estimated by its conversion into indigo blue.

Among the coloring matters a similar substance was observed by Heller, and named uroxanthine, but it has since been found to be identical with indican.

Its presence can be detected by the method of Jaffé modified by Senator.

Pour two drachms (7.775 c.c.) of urine into a test-tube, and add an equal quantity of fuming hydrochloric acid, and then a concentrated solution of chloride of lime, drop by drop, until a blue color is fully developed. Shake the mixture with two drachms (7.775 c.c.) of chloroform, which will sink to the bottom and be more or less deeply tinged with indigo if indican be present.

The quantitative test of Jaffé is too complicated to be of any practical value.

Indican is said to be always present in normal urine, but in very small quantities. By different observers it has been found to be increased by a meat diet, carcinoma of the liver, cholera, cholera morbus, diarrhœa originating in the small intestines, markedly in obstruction to the small, and slightly with obstruction to the large intestine, in Addison's disease, with nervous exhaustion, especially affecting the spinal cord, in urina spastica, frequent coitus, onanism, etc., and with every irritation to the urinary tract, nephritis, Bright's, uræmia, typhoid and intermittent fever, etc.

Clinical significance.—From this large list of different conditions, to which many others in all probability could be added, it is almost impossible to draw any practical deduction, except that it indicates an increased and possibly incomplete proteid metabolism.

It has been suggested as a means of diagnosticating lesions of the small intestine or occlusion of its lumen; but since so many other conditions produce a like result, much of its value is lost. If its quantity

could be easily calculated, it might be an element in differentiation between a lesion involving the large and small intestine; but, owing to the time required and the uncertainty of the result, it can hardly be considered as affording reliable proof in so acute a condition as obstruction to the lumen of the small intestine. Theoretically, it is a very nice point of differential diagnosis, but, practically, the patient might easily die before a positive result could be obtained.

CHAPTER VI.

URATES, PHOSPHATES, AND CHLORIDES.

URATES.

The uric acid may be combined with soda, ammonia, potash, lime, or magnesia, forming a urate. The urates of ammonia and soda are the most common and may be either neutral or acid in reaction.

These salts occur in high-colored urine when the quantity is diminished and its density increased.

Such urine when first voided is clear, but on cooling becomes cloudy or a decided deposit is developed. The sediment may be only a faint cloud, or it may be nearly white, a deep pink, or a decided reddish deposit. The latter, when abundant, is known as the brick-dust deposit.

They are usually only deposited in acid urine, but may at times be found in faintly alkaline samples.

The urates have to be distinguished from the phosphates and albumin.

They are distinguished from the former by heat, which precipitates the phosphates and dissolves the urates; alkalies and the carbonates also dissolve them, the reverse being true of the phosphates.

From albumin they are differentiated by heat and nitric acid, which causes the urates to disappear and the albumin to be precipitated.

The white urates of children might be mistaken for the phosphates, but the above tests will at once decide the question.

Occasionally, when the urine is very concentrated and the urates unusually abundant, they may be deposited almost as soon as they are expelled; but, as a rule, the sample must cool before they make their appearance. Normal urine at a very low temperature will generally deposit the urates.

There is no evidence that certain kinds of food increase their formation, but incomplete digestion, absorption, and assimilation from any cause which interferes with the perfect nitrogenous transformation promotes their development to an unusual degree.

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They appear to be increased, not so much by a large production of uric acid, as by its incomplete formation.

In all forms of acute diseases, such as pneumonia, typhoid fever, and all conditions accompanied by increased bodily temperature, the urates are abundant. As the disease improves and the physiological processes become more completely performed, they gradually decrease in quantity.

The same is true in gout; during the attack they are abundant, as the patient recovers they disappear. In gout, it matters little what kind of diet is allowed, provided it is cut down to the limit of perfect transformation and assimilation by the diseased system. This is the explanation for the ready recovery of a gouty patient upon a purely nitrogenous diet. In most cases, the rightly adjusted mixed diet will afford the most satisfactory results. In other cases, the very presence of the starches and sugars are the causes which prevent the perfect proteid metabolism and retard recovery. In such a case, a purely nitrogenous diet will produce a cure where the most judiciously selected mixed or an exclusive non-nitrogenous diet would continually make the disease worse. Consequently each case must be separately analyzed and treated accordingly.

In the urine of children when teething, an abundant, white deposit of the urate of ammonia is not of infrequent occurrence, and has often been mistaken for a phosphatic deposit.

The urates are occasionally found in excess after any severe mental exertion, physical exercise, or profuse perspiration, and indicate only a physiological change.

With organic disease of the viscera and especially the liver, or with an incompletely performed gastric, intestinal, and hepatic digestion, the urates appear in the urine in abundance.

Clinical significance.—From the above-enumerated causes and conditions, only one conclusion can be deduced; which is, that the urates are only of importance when they are continuous, and in all cases indicate an incomplete metabolic transformation of the proteids which has chiefly to do with a faulty action on the part of the liver.

Treatment.—The most speedy and certain relief will follow a well-regulated diet, plenty of out-door exercise and possibly the addition of some of the numerous cholagogue tonics.

PHOSPHATES.

These salts occur in pale urine of alkaline reaction and diminished density. The phosphoric acid is combined with soda, lime, or mag-

nesia, forming a phosphate. The two former may be combined in such a way as to form an acid or alkaline salt.

Heat, when applied to faintly acid urine, will drive off the carbon dioxide (CO_2), and if the phosphates are present in abundance the fluid will become turbid. Such samples may be mistaken for those containing albumin, but one drop of nitric acid will dissolve the salts and cause an albuminous precipitate to become more apparent. In this way the two can at once be distinguished from each other.

Heat precipitates the phosphates, but causes the deposit of urates to disappear. The phosphates occur after alkaline fermentation has been developed. The urine may be cloudy, when first voided, from the presence of the phosphates.

Clinical importance.—The phosphate of soda and potassa are always in solution, but the phosphate of lime may form an amorphous or crystalline deposit. The phosphate of magnesia may also form a crystalline deposit.

The phosphates are derived both from the food and the metamorphotic changes going on in the body. During the early stage of all inflammatory conditions while the exudation is being poured out, they are decreased in the urine, but after this stage they progressively increase, and with the subsidence of the process they decrease to the normal standard. The same phenomenon is noticeable in connection with all acute febrile conditions. In meningitis, the same disappearance, rise, and fall has been observed. A similar change has been supposed to occur in connection with excessive mental strains and in certain forms of indigestion. But as yet no very definite clinical data are to be derived from the study of these ingredients. In relation to the above-named inflammatory conditions and acute diseases, the chlorides bear about the same relation, and being more easily estimated yield all the practical information required.

With a highly vegetable diet, with injuries to the spine, in mania and with many nervous disorders, as well as in elderly people, the hepatic functions will be incompletely performed. With such conditions there is apt to be an incomplete formation of uric acid and consequently a fall in the acidity and apparent increase of the phosphates in the urine. In fact, the urine may become continuously alkaline, the deposition of the phosphates persistent, and a formation of a phosphatic calculus almost certain. It is of importance to recognize this condition, as the treatment depends wholly upon the property of forming uric acid, and every measure should be instituted that will increase the total quantity of this acid formed.

An opposite condition or over-acidity may give rise to alkaline urine

and a deposition of the phosphates. This is brought about by the over-production of uric acid which irritates the genito-urinary tract, excites a decomposition of the urine, alkaline fermentation, and the precipitation of the phosphates. With this variety the urine will previously have been highly acid.

The treatment for this is directly opposite to that for the previous condition. The production of the uric acid must be decreased.

The urinary symptoms being nearly the same, a close study of the clinical symptoms and the digestive processes in general are absolutely essential for a differential diagnosis between the two.

With obstructive lesions to the urinary tract, with partial retention and alkaline fermentation, the same alkaline urine with a phosphatic deposit will be observed. Here the condition is, more strictly speaking, a local one, and has to be treated as such, and when treated in connection with a regulated diet the difficulty is soon relieved.

CHLORIDES.

Chlorine is found in the urine combined with potassium, ammonium, and sodium. The last, however, is the salt of special interest.

A nitrate of silver solution is the most practical for both quantitative and qualitative analysis.

Liebig's volumetric process with a solution of nitrate of mercury, or Mohr's with nitrate of silver, are undoubtedly the most accurate tests, but too complicated to become generally useful.

For a complete description of those tests the reader is referred to more extended works.

For practical work, a standard nitrate of silver solution is made by adding one part of nitrate of silver to eight parts of distilled water.

Before testing for the chlorides, the urine should be acidulated with a few drops of nitric acid to prevent the precipitation of the phosphates which otherwise would occur.

Add one minim of the silver solution to the sample of urine to be tested. If the suspected solution still remains clear and transparent, it indicates the total absence of the chlorides.

If the solution becomes generally, but only slightly turbid, it indicates the presence of one-tenth of one per cent of the chlorides.

If cheesy lumps are deposited and the supernatant fluid and precipitate remain unchanged, the chlorides are present in quantities ranging from one-half to one per cent.

The normal amount of chloride of sodium discharged in the urine,

admitting that 200 grains (12.959 gram) are eliminated daily in 50 ounces (1555.174 c.c.), would be a fraction over one-tenth of one per cent. Consequently the slightest increase or decrease will be readily appreciated by the above solution. If we allow a smaller quantity than normal, there is apt to be a precipitate, for then the quantity remaining is sufficient to cause a cloud.

The chlorides, like all other normal ingredients of the urine, are subject to wide variations dependent upon the quantity taken into the system daily and the amount of water eliminated.

In health, the taking of an excess of the chloride of sodium is not indicated by its increase in the urine for several days, and after its use is discontinued it takes several days for it to disappear, hence an accumulative action is observed. This, however, does not appear to be the case in disease.

Fortunately for this test, the urine is usually decreased in quantity which readily renders the increase in the chlorides very apparent.

If fifty ounces (1555.174 c.c.) be taken as the standard daily secretion of urine, it will be easy to compute the comparative quantity of solids present, by evaporating down the whole amount if it exceeds that number, or by diluting it with distilled water if it has a less volume.

Clinical significance.—In all acute inflammatory processes where there is a marked fibro-plastic or serous exudation, the inflammatory deposit is usually found to contain an abundance of the chlorides, phosphates, and carbonates, and at the same time they are deficient or absent in the urine.

The diseases in which they are especially important are pneumonia, typhoid fever, pleurisy with effusion, cholera, and in fact in all acute febrile conditions, especially if there is much exudation. Their reappearance in the urine is always indicative of improvement or of the reabsorption of the inflammatory exudation, other things being equal, and often tells of approaching recovery when all the clinical symptoms remain apparently unchanged.

If, on the other hand, after returning in the urine they should suddenly disappear or become greatly diminished in quantity, while the clinical symptoms apparently remain about the same, it is always a bad omen and indicates an exacerbation, due to an extension or the development of a new inflammation, and renders the prognosis unfavorable.

Consequently, by a daily examination for the chlorides in severe cases of pneumonia, where the patient is too feeble for a satisfactory physical examination, valuable information may be obtained, and it

will enable the attendant to prognosticate and treat the case more intelligently.

One very important fact to be remembered is, that the physician often is not called to see the case until the height of the inflammatory process has been reached, and therefore there will be no time when the chloride of sodium is absent from the urine, for it has already begun to be reabsorbed and eliminated.

The most important clinical fact is, as to whether it continues until the marked rational symptoms indicative of recovery have been developed. By observing these conditions, the physician can always be in advance of the ordinary symptoms with his treatment.

The examination for the chlorides is most important in pneumonia, on account of the extensive exudation, but should not be neglected in any severe or acute inflammatory disease.

A peculiar cloudiness spontaneously forming in the urine, in cases of severe fevers, has by some observers been found to indicate an almost certain restoration to perfect recovery. Although unexplained by them, it is probably due to the abundant reappearance of the urates, phosphates, and chlorides.

CHAPTER VII.

ADVENTITIOUS COLORING-MATTERS; BILE PIGMENT; FAT; MUCUS; BLOOD OR HÆMOGLOBIN.

ADVENTITIOUS COLORING-MATTERS.

Under this heading, a large number of substances will be mentioned, most of which have been considered at some time as the true coloring-matter of the urine, while a few have been classed as derived pigments. Their large number and diverse nature will at once show the uncertainty existing in the minds of the chemists as to the true coloring-principle of urine.

They are: 1st, the urochrome (Thudichum); 2d, indigo, of which there are three varieties described: the white, red, and blue. The white form is also called, 3d, indican (Shunk) or, 4th, uroxanthin (Heller); it is capable of being converted into red indigo or, 6th, urrhodin (Heller), or into blue indigo; 7th, indigotin or, 8th, uroglancin (Heller); 9th, urohematin (Harley and Scherer); 10th, urobilin (Jaff); 11th, hydrobilirubin (Maly); 12th, purpurin (Bird and Prout); 13th, uroërythin (Heller, Bird, and Prout); 14th, urophœpne (Heller and Ziegler); 15th, urian (Shunk); 16th, urianin (Shunk); 17th, uromatin (Harley); 18th, cyanourin (Braconnot); 19th, urrhodinogen (Thudichum); 20th, uromelanin (Thudichum); 21st, uropittin (Thudichum); 22d, chromogen (Thudichum); 23d, urosin; 24th, urosacin; 25th, hemophin; 26th, melanogen.

Many of these are synonyms, the same or an almost identical substance having been discovered at about the same time and independently named by each discoverer. Many others are derivatives from some more fixed pigment.

The three of importance are urohæmatin, urochrome, and the indigo forms. The former is unquestionably the primary source of a large number of this list, which under different analyses have yielded a slight difference in the atomic formulæ. Urohæmatin or urochrome—the latter name being preferable—is, in all probability,

derived directly from the coloring-matter of the blood, and is the substance which gives its peculiar yellow color to the normal urine.

The tests for these substances are based upon colors or shades of color, or on extended chemical analysis, both being impracticable in general medicine.

Indican as a coloring-matter has been found to be increased in the urine in such a wide range of diseased conditions, and its detection and quantitative analysis are so uncertain, as to render its presence or absence of little practical importance (see page 271).

Clinical significance.—The dark, reddish-yellow color of the urine with all forms of fevers is ascribed by Heller to uroërythin and an increase in the normal coloring-matter, but there is some doubt about uroërythin being a special coloring-substance developed as the result of disease; it appears more likely to be a derivative of urohæmatin, and the color of the urine and its variation in disease is better explained under the hæmatoglobinuria theory, which may cause a number of slightly different pigments to be discharged, as a result of the rapid destruction of the hæmoglobin.

BILE PIGMENTS IN URINE.

The *biliary coloring* matters are the only other pigments of real importance. They give to the urine varying shades of color from brown to green.

The test for them is Gmelin's bile, or the nitro-nitrosic acid test. It is employed as follows: place some of the suspected urine on a clean white porcelain dish, then add a few drops of nitric acid containing a good proportion of nitrous acid until the two run together. Radiating from the point of contact, there will be observed the following play of colors, green, blue, violet, red, and last a dirty yellow.

If biliverdin only be present, the green is absent, and the play of colors will then be blue, violet, red, and dingy yellow.

Brück's test is as follows: Pour the suspected urine on a white porcelain plate, add a few drops of dilute nitric acid, and then some strong sulphuric acid instead of the nitrous acid. The same play of colors will be the result. A test-tube can be used instead of the plate if found more convenient. The contrast of colors, however, will not be so striking as is the case with a white background.

The fluid should be absolutely free from alcohol, as this will cause an abundant formation of nitrous acid, and the same color rings, even in the absence of bile pigment.

Indican in the urine may lead to an error, but by making sure that the green, blue, violet, and red are all present in regular order, no

mistake will be made, for the indican only produces green and yellow zones under the same circumstances.

In cases of long-continued high temperature, bile pigments may be present in the urine, and yet not respond to the tests; the reason for this has not been explained.

In such instances, if it is necessary to determine the presence of bile, Huppert's method may be used; this is as follows: Precipitate the urine with milk of lime, and filter. Take a piece of the precipitate, of the size of a hazel-nut, and place it in a test-tube, and fill the tube half full of alcohol, add sulphuric acid until it retains an acid reaction after shaking. Warm this fluid, and the color will be extracted from the precipitate; filter and boil the filtrate. If bilirubin is present in the urine, it will combine with lime and be precipitated; the acid will set it free, and it will be dissolved by the alcohol, forming a yellowish-green solution. The more acid the quicker the response. Long boiling may produce a blue color.

Why this reaction is not due to the alcohol as in the other case is not explained, and possibly this may be the source of the reaction and not the biliary pigments.

Many oxidizing agents will produce various shades of green when applied to urine containing bile pigment. Iodine and atmospheric air produce a grass-green. A pure caustic potash solution, strength one part to three of water added to urine, with an excess of hydrochloric acid, will produce an emerald green color if bile pigment be present. (*Ultzman's test.*)

Clinical significance.—Bile pigment may be found in the urine in a very large number of diseases, viz., obstruction to the ductus communis choledochus or its hepatic tributaries from any cause, and in cases without obstruction, such as poisoning by the various severe fevers in which jaundice is a common symptom. It is also observed in yellow, malarial, and relapsing fevers; and with typhus, some cases of typhoid, scarlatina, small-pox, acute yellow atrophy of the liver, epidemic jaundice, and pneumonia; also with animal poisons, such as pyæmia, septicæmia, puerperal fever, rabies, snake bites, etc.; and again in connection with poisoning by the minerals, phosphorus, mercury, copper, antimony, and with chloroform and ether, and after severe mental emotions, fright, anxiety; concussion of the brain, asphyxia, excessive production of bile, congestion of the liver, etc.

Gmelin's test is unquestionably the most practical, but from the large range of conditions giving rise to the appearance of bile pigments in the urine, little practical importance can be attached to it.

The presence of bile pigment in the urine, however, may be said

to be indicative of one of three things: an occlusion of the bile ducts, an over-production, or an inability on the part of the system to completely reconvert the constantly reabsorbed pigment.

In functional derangements of the liver, it is quite important to know whether there is a deficient or an over-production of bile, and the presence or absence of these pigments may be turned to accoun in helping to decide the question.

When there is a deficient production both in quantity and quality, bile pigment will not be apt to appear in the urine, but with over-production it is quite likely to be found.

FATTY MATTERS.

Fat is rarely seen in the urine except in cases of chyluria. Accidental cases, however, are excepted, for it is not uncommon that the specimen brought to the examiner is in a dirty bottle, which has contained some oily matter.

Test for fat.—Agitate fresh urine with an equal volume of sulphuric ether in a narrow cylinder, and let the mixture stand for twelve or twenty-four hours. It will separate into three parts, a superior of ether, and an inferior of urine, while between the two there will be a thin yellow oily layer. The sample, which previously was milky, will become perfectly clear. This oily layer may be siphoned or decanted off.

Evaporate the ether from the fluid removed, and the result will be little yellow globules looking like butter, and often having a rancid odor. This fatty material, on the application of a gentle heat, will melt into a yellow oil which slowly solidifies on cooling.

Fat occurs in the urine as the result of epithelial disintegration in some forms of chronic renal disease, but even then it only occurs in microscopic quantities.

MUCUS.

This substance usually occurs in the normal state as a faint and indistinct cloud after the urine has stood a few hours. It is most abundant near the bottom of the fluid and especially in the urine of the female.

The chemical test for mucus is to add *acetic acid* drop by drop until fine fibrillated bands of mucus, which are often tortuous in outline, begin to fall.

By adding a little iodine or iodide of potash with the acetic acid,

these delicate bands of mucus which are thrown down are rendered more visible.

Tartaric acid and very weak solutions of the mineral acids will give the same reaction. The precipitate in all cases is dissolved by an excess.

These tests are rather uncertain. The cloud which is seen to form in the fluid is quite as certain evidence of the presence of mucus.

Clinical significance.—Continued irritation of the urinary tract without inflammation and the formation of pus will often increase the mucus to an easily perceptible amount. Usually, however, the increased quantity is associated with an inflammatory condition and the more or less abundant formation of pus.

With such conditions as a urethritis, catarrh of the bladder, cystitis, ureteritis or pyelitis, the mucus is often very abundant, forming large and tenacious ropy strings in the urine. It is also present in large quantities in cases of metritis and vaginitis.

BLOOD HÆMOGLOBIN.

It sometimes happens that after a hemorrhage from the urinary tract the corpuscles are dissolved and cannot be found by microscopic examination. In hæmoglobinuria, few if any corpuscles are found. In such cases it may be necessary to employ a chemical test for the detection of the presence of blood. The *guaiac* or *Heller's test* may be used.

The *guaiac test* is employed as follows: Add a few drops of the tincture of guaiacum to a small quantity of urine in a test tube; then add about as much ozonized ether (a solution of peroxide of hydrogen in ether) as there is urine. If blood-coloring matter be present, a sapphire blue color will be produced.

Another method is to add equal parts of tincture of guaiacum and oil of turpentine in a test-tube to an equal volume of urine; if blood be present a deep blue color is produced.

Heller's test.—The urine is rendered alkaline with liquor potassa or soda, heated to the boiling point, and set aside. The precipitated phosphates are of a greenish or reddish color if the blood-coloring matter, hæmoglobin, be present.

Spectroscopic examination, however, is the only certain method by which the presence of the blood-coloring matter can be detected, but this is not convenient for ordinary use.

Clinical significance.—The appearance of dissolved blood-corpuscles or soluble hæmoglobin in the blood is found chiefly in hæmoglobinuria

and is only of importance in such cases. If its presence could be easily ascertained, and if present in minute quantities, it might be of great service in all cases of high-colored urine in showing whether the color represented blood destruction or was due to some other cause.

CHAPTER VIII.

HOW TO USE THE MICROSCOPE; RED BLOOD-CORPUSCLES; LEUCOCYTES; MUCUS.

How to use the microscope and mount samples.—The instrument should have a solid base, and be placed upon a firm, but rather low table. The direct rays of the sun should not be used for illumination. A north light is generally considered the best. If good daylight is not to be obtained, a small kerosene hand lamp will answer sufficiently well. A student's lamp will give a very perfect light.

It is always best to look through the instrument with both eyes open; at first this will be impossible, but a little practice will soon overcome the difficulty.

Of the two reflecting mirrors, the concave is the one most used in urinary examinations.

The best combination for urinary work is a good $\frac{2}{3}$ inch objective which will magnify the object from 60 to 100 times; and a good $\frac{1}{5}$ or $\frac{1}{6}$ objective which will magnify the object from 250 to 400 times. With these lenses a medium eye-piece should be used.

Every instrument should be furnished with a "nose-piece," a brass attachment which is screwed into the end of the barrel and carries two or more lenses on a revolving arm. By it the lenses can be shifted almost instantaneously, and in this way much time is saved. A general survey should be made with the low power and then the special object resolved with the high power.

The first thing to be acquired in using the microscope is to learn how to arrange the mirror so as to get the direct reflection of the light through the lens, tube, and eye-piece. This is accomplished by shifting the mirror until the right angle is obtained.

The next step is to learn how to focus the instrument upon the object to be examined. As the working distance between the face of the lens and the cover glass is only a small fraction of an inch, considerable difficulty is often experienced by the beginner.

The object having been mounted and placed on the stage, the barrel is caused to descend until the objective is brought nearly down to the

cover. The examiner now looks through the eye-piece and gradually lowers the barrel, at the same time following it down with his eye until blurred objects commence to appear in the sample. Then by changing from the coarse to the fine adjustment a few turns of the latter one way or the other, as may be required, will bring the object distinctly into focus; at the same time the slide is held or moved at will with the opposite hand until every object has been completely studied. This rule should invariably be adopted: with one hand keep the fine adjustment screw in motion so that every part may be accurately focussed; at the same time keep moving the slide until every part under the cover glass has been brought into the field of vision. In this way a thorough analysis of the sample is made.

Urinary sediments are usually most abundant near the margin of the cover-glass. If there is danger of missing the objects sought after, a strip of tissue or filter paper may be laid at the edge of the cover on one side, which will cause a current and float the solid particles over to that edge of the cover, when they can easily be found.

The next step is to mount the object. The necessary implements are slides, cover glasses or circles, pipettes, and a pair of small forceps.

The cover glasses should be thin and scrupulously clean. A 4% solution of acetic acid will be found the best liquid to remove all grease and by rubbing with a silk handkerchief, old linen, or tissue paper, they can be rendered very free from dirt. After cleansing, they should be handled with the forceps, or by their edge only if the fingers are to be used. Finger marks on the surface are seen as foreign objects.

The best pipettes are made from quarter-inch glass tubing, which should be cut at right angles at both ends and never pointed. A square end pipette is much better than a tapering extremity, for the reason that there is a much larger space to draw the sediment through. The length of the tubes may vary from six to ten inches (15 to 25 centimetres). For crystals and heavy deposits, one finger is placed over one end of the pipette, while the free extremity is passed to the bottom of the vessel containing the sediment, and then the finger closing the opposite end is quickly removed. The finger is then replaced and the pipette and its contents quickly withdrawn from the fluid. By this method the solids are caused to run rapidly up into the lumen of the tube in considerable quantities. One or two drops should be allowed to escape and then one should be secured on a perfectly clean slide. The main object is to gauge the drop so that it will be just covered by the circle used and none allowed to flow outside. If there is too much,

the cover glass may float and be kept in constant motion, or all the sediment washed out. Too small a drop is preferable to an unduly large one.

The circle should now be placed over the sample. This is best accomplished by seizing one edge with the forceps; then place the under side of the opposite edge first on the slide near the drop, then bring it in contact with the urine, followed by a sliding motion so that the under surface of the cover may be moistened. Then gradually let down the side held by the forceps. By following this rule, the formation of air-bubbles under the circle is prevented. The specimen is now ready for examination.

If casts are to be looked for, the pipette is used in the same manner as before, with this exception, viz., instead of going deep into the deposit, the introduced end should be stopped just at the superior border or a little above the sediment, and, instead of letting the fluid rush in rapidly, the finger should be removed cautiously so that the sample will run in gradually. By moving the tube around, the examiner can often skim off the top of the solid portion. It should be mounted as before. The reason for this method is that casts, being lighter than the other solid ingredients, collect on the top of the apparent sediment, where they are most abundant and consequently they are more likely to be secured at this point.

A failure to observe this important rule in many samples containing large numbers of casts results in their being overlooked and reported by the examiner as absent. Repeated trials should be made before saying that casts are or are not present.

Never return the contents of the pipette to the sample under examination, as it will stir up the sediment and prevent any further satisfactory search until several hours have elapsed.

BLOOD-CORPUSCLES.

The red blood-disks only will be dealt with at this time. Under the microscope the normal corpuscle will be found to be perfectly round, and very faintly tinged with yellow by their contained hæmoglobin. If only one disk be present in the field, it is at first hard to recognize or to distinguish any color, but concentration and comparison with other objects will usually enable the examiner to appreciate its presence. If a number are collected together, the color is quite apparent, and if abundant, a distinctly reddish tint is plainly seen. Their average diameter is $\frac{1}{3600}$ of an inch, 6.9 mmm. The red disk is biconcave and consequently is thicker toward the periphery than at the centre or free margin. The result is that it has two focal

centres.   When the rim is in exact focus, the centre appears as a dark
spot surrounded by a light zone which in turn is encircled by a dark
ring representing the thin margin.   When the centre is in exact focus,
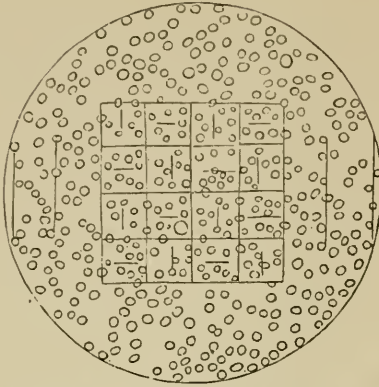
FIG. 56.—BLOOD-CORPUSCLES AS SEEN WITH THE SQUARE OCULAR MICROMETER (Keyes).

it will be light and transparent, surrounded by a single broad and
dark band of considerable width.   This peculiar optical property has
led occasional observers to believe that the red corpuscles contained a
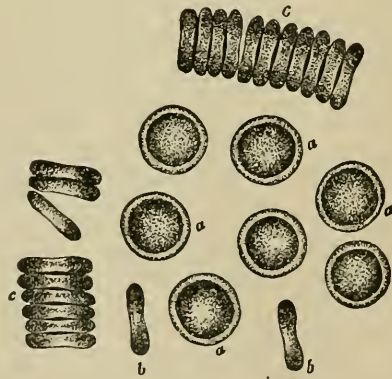
FIG. 57.—HUMAN BLOOD-CORPUSCLES.

a, Globules showing double contour; b, globules turned on edge; c, the same in rouleaux, like
coin. Highly magnified (Rollett).

nucleus, which, however, is not true, but is a microscopic delusion.
By exciting a current in the fluid while looking at them, they will be
seen to turn on their edges, when their biconcavity becomes more

easily appreciated. When very abundant, they sometimes adhere together by their flat surfaces like rolls of coins and are known as rouleaux.

In urine, they are likely to undergo destructive changes and become altered in character. If the watery element of the urine is abundant, the hæmoglobin will absorb it and cause the corpuscles to swell, become spherical, lose their color, and finally disappear altogether. Just before dissolution they often appear like rings or shells (Fig. 58, *b*). Strong alkalinity of the urine produces a like result. If deprived of their water, they become shrivelled and shrink, forming irregular star-shaped or crenated disks. After having undergone this transformation, they are hard to recognize by those not familiar with this change. The red corpuscles sometimes undergo slight amœboid movements.
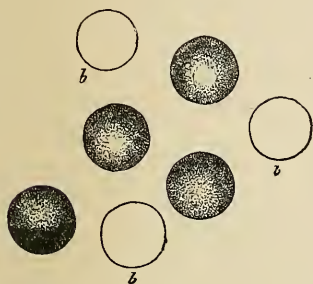
FIG. 58.—HUMAN RED BLOOD-GLOBULES.
a, With hæmoglobin; *b*, without hæmoglobin.
Highly magnified (Rollett).
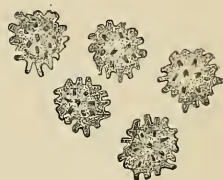
FIG. 59.—HUMAN BLOOD-CORPUSCLES
CRENATED.
Highly magnified (Rollett).

Clinical significance.—Blood-corpuscles may be found in the urine after any operations on and in the immediate vicinity of the genitourinary tract. They may occur with urethral stricture or stone, calculi in the bladder, ureters, or pelves of the kidneys. Also with inflammation of the urethra, bladder, ureters, or renal pelves and kidneys; and with villous, sarcomatous, or carcinomatous tumors of the bladder.

Blood in the urine is also found in cancer, sarcoma, and tubercle of the kidneys, suppurative nephritis, irritation by crystals in the kidneys, acute diffuse nephritis, and in some of the other forms of nephritis; in purpura hæmorrhagica, scorbutus, scurvy, pernicious anæmia, leucocythæmia, eruptive fevers, yellow fever, continued and malarial fevers, acute and chronic congestion, injury with or without rupture of the renal tissue or urinary tract, emboli, thrombosis, and infarc-

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tion of the renal vessels, phthisis, wasting diseases, and parasites of the kidneys.

In females, it is found during menstruation, pregnancy, and in connection with uterine diseases.

Certain irritative medicines, viz., turpentine, cantharides, squills, and all irritating diuretics will cause it.

Some consider blood in the urine quite diagnostic of certain forms of chronic kidney lesions; but experience has shown it to be present occasionally in all forms.

From this very long list of causes for blood in the urine, there are few, if any, cases in which its origin can be positively stated.

If blood casts are found in the sample, it is positive evidence that some of the blood came from the kidneys. With severe injuries and symptoms of injury to the kidneys, the presence of blood in the urine would strengthen the diagnosis of rupture of the organ. But hemorrhage may occur after injury and no laceration be found at the necropsy.

Clots of blood indicate external hemorrhage or blood from the urethra or bladder.

LEUCOCYTES.

This term, for convenience and the inability to differentiate between the white blood-cell, a mucus, and a pus corpuscle, is applied to all.

When they are examined in an indifferent fluid, the following appearances will be observed:

The white blood-corpuscle is a round granular body from $\frac{1}{3000}$ to $\frac{1}{2500}$ of an inch (10 to 8 mmm.) in diameter, in which the nucleus is faintly visible.

FIG. 60. — ORDINARY APPEARANCE OF PUS.

The mucus-corpuscle is about the same size, and has a granular appearance and a little more distinct nucleus.

The pus-corpuscle also has about the same size and appearance; if any difference exists, it is a little more granular.

The differences, if any, may be stated as follows:

1. *White blood-corpuscles,* nucleus least distinct.
2. *Mucus-corpuscles,* nucleus most distinct.
3. *Pus-corpuscles,* granular appearance most distinct.

These variations are more theoretical than real. Even under the most favorable circumstances it requires a skilled observer to appreciate these fine points of distinction. Withdraw the favorable conditions, and replace them by the opposite and also degenerative changes

to which they are constantly subject, and it becomes absolutely impossible to tell one from the other.

Some observers go so far as to say that there are marked differences in the same kind by which varying grades of constitutions can be detected, and an accurate diagnosis and prognosis established. This, however, seems impossible from the great difficulty to isolate such cells normally, and the many retrograde changes they are likely to undergo from the time of development to the time of examination.

All that can be said with any degree of certainty when they are found in the urine is that there is a catarrhal or inflammatory condi-
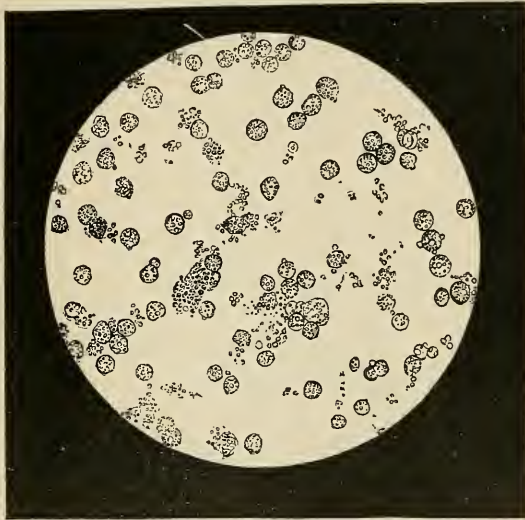
Fig. 61.—Pus in Various Stages of Development.

tion of the genito-urinary tract, or that the contents of a pus basin have found their way into the sample of urine under examination.

When any of these corpuscles are in aqueous solutions, they tend to imbibe the water, swell up, and become less granular, or even transparent. In too concentrated solutions, they give up their water and shrink.

In the former case, the nuclei will be a little more transparent; in the latter, they are still more difficult to find.

If they are acted upon by acetic acid, the granules tend to leave the body of the protoplasm and accumulate in the nucleus. This causes an opacity of the nuclei and clearness of the remaining portion, so that the nuclei now stand out in bold relief. The number of nuclei

will depend upon the rapidity and incompleteness of their develop-
ment. If the formation has been slow and as near perfect as pos-
sible, not more than two nuclei will be found, but with a more rapid
production, three, four, five, six, or more will make their appearance,
and be found in one protoplasmic mass. This reaction of pus-cells
with acetic acid is very marked, and confirms the diagnosis.

The many changes in the reaction of the urine are a fruitful source
for variation in these corpuscular elements. From hour to hour they
may undergo changes which will materially alter their general char-
acter.

Frequent expectoration into the chamber is not an uncommon
cause for leucocytes of the mucus variety in the urine.

These white corpuscles often exhibit marked amœboid movements.

Leucocytes may be found in the urine in quantities varying from
one to hundreds to each slide examined.
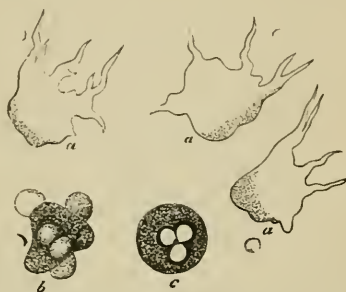
FIG. 62.—HIGHLY MAGNIFIED LEUCOCYTES.

a, Putting out processes; *b*, having withdrawn processes (Rollett).

Clinical significance.—Their presence indicates a gonorrhœa, gleet
stricture of the urethra, prostatitis, prostatic abscess, catarrh of the
bladder, tumors, pyelitis, pyelonephrosis, cancer and tuberculosis of
the kidneys, also renal calculi.

In large quantities they are indicative of a cystitis, pyelitis, or a
pyelonephrosis.

In the female, they may come from the vagina or uterus.

MUCUS.

This substance is very frequently seen in microscopic examinations
of urinary samples, and, on account of the frequency with which it is
confounded with casts, it is of no little importance.

It usually occurs as delicate films or streaks, which may run more

than across the field of vision. Their outlines are more or less irregular, and at places almost invisible. By following one of these bands along its course, it will often be found to terminate in an irregular mass of mucus. This in itself would distinguish it from a cast. In other cases, its ends become more and more irregular and ragged, and are ultimately lost in the fluid. Their exact point of termination is often indefinitely marked.

By some writers, mucus casts or plugs are described and said to come from the renal and seminal tubules and the follicles of the prostate gland.

They are described as long mucus plugs which are often branched, and when they are generated in the seminal tubes are said to have associated with them spermatozoa. This peculiar formation, as ordinarily represented by Whittaker's plates, has never been observed by the author.

CHAPTER IX.

URIC ACID, OXALATES, URATES, PHOSPHATES, MICROSCOPIC PIGMENTS.

URIC ACID.

When absolutely pure, this acid is a crystalline substance without color. The crystals are of many shapes and compound forms. They may be rhombic, lozenge, spindle, barrel, or even dumb-bell in shape, or they may form tables, prisms, and long and short rods. They may also be deposited as stars, or by an aggregation of some of the simple

FIG. 63.—IRREGULAR AND DUMB-BELL CRYSTAL OF URIC ACID.
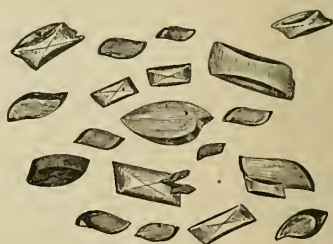
FIG. 64.—IRREGULAR FORMS OF URIC ACID CRYSTALS.

varieties develop into stars, bundles, or even balls and spikes, or spiked crystals.

Their distinguishing feature in the urine is that they are almost always colored. It may be only a faint yellow tint, but the rule is a decided reddish or brown shade.

The crystals may be easily recognized by the naked eye, but under ordinary circumstances the color is clear and decided, making them easy of recognition. There is nothing else in the urine that they can be mistaken for. Their clinical significance has already been noted (p. 264).

In rare instances they do not become colored, but retain their

normal whiteness, and are then known as the white crystals of uric acid.
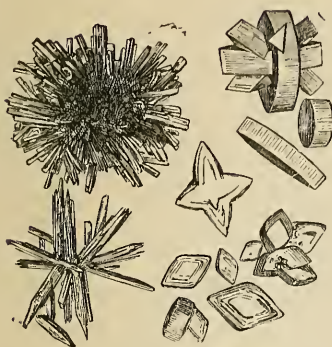
FIG. 65.—URIC ACID ROSETTES.

FIG. 66.—URIC ACID ROSETTES AND IRREGULAR FORMS OF CRYSTAL.

OXALATE OF LIME.

It was once believed that oxalic acid did not exist free in the human system, but of late it seems to have been proven that it does, and that it is eliminated from the blood in its pure form. It, however, most

FIG. 67.

FIG. 68.
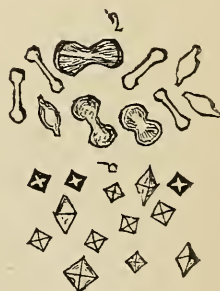
FIG. 69.

OXALATE OF LIME CRYSTALS.

67, Ordinary forms; 68, typical forms, rectangular octahedra; 69, irregular and dumb-bell forms.

frequently occurs in the urine in combination with calcium, forming the lime oxalate crystals. Their typical form is rectangular octahedra, but anomalous forms are occasionally found having the form of amorphous lumps, dumb-bells, or square columns with pyramidal ends.

They are insoluble in water, alcohol, ether, ammonia, alkalies, and acetic acid, but are soluble in the mineral acids, and to some extent in sodium phosphate and urate.

From uric acid they are distinguished by their insolubility in alkalies, and from the phosphates by their insolubility in acetic acid.

Under the *microscope* they appear as minute, little squares with cross markings and of a pure white color, resembling somewhat a folded square envelope. In size, they range between $\frac{1}{5600}$ to $\frac{1}{500}$ of an inch, 4.535 mmm. to 50.679 mmm.; the latter are rarely found, the small size usually predominate. The dumb-bell forms are infrequent, and range in size from $\frac{1}{1500}$ to $\frac{1}{600}$ of an inch, 16.933 to 42.332 mmm. The other forms are also rare. If a side view is obtained, the most common shape is the octahedron, or double pyramid, two pyramids base to base.

They might be mistaken for some of the uric acid forms, but the color will establish their character, and the size will differentiate between them and the triple phosphate.

Urine containing oxalate of lime is always acid, of an amber tint, and contains finely cloudy mucus.

Oxalates in the urine may be the result of certain kinds of vegetable food that contain an abundance of oxalic acid, from an incomplete metabolism of the waste products of the body, or from deoxidization of urea and uric acid, as in urine from acid fermentation. Some appear to have proven that they come directly from pre-existing oxalic acid in the blood joining with the lime, either in the blood or the protoplasm of the epithelial cells lining the uriniferous tubules, more probably in the latter.

This method of formation helps to explain their presence in the uriniferous tubules and in the substance of the cells.

Clinical significance.—The presence of oxalate of lime crystals in the urine does not appear to be characteristic of any particular disease. They are, without doubt, the result of mal-assimilation, which can generally be traced to an incompletely performed hepatic digestion and one in which there is an over-production of a poor quality of bile. If they are deoxidized or incompletely oxidized urea or uric acid as some believe, it still argues in favor of the primary difficulty being located in the liver.

With nervousness, hypochondriasis, dyspepsia, and indigestion they make their appearance in the urine, and also in some forms of renal colic, forming a calculus by being aggregated together (mulberry calculus).

The most satisfactory treatment is plenty of open-air exercise, with

a free administration of dilute nitro-hydrochloric acid. But foremost of all is a strict attention to the diet and digestive functions.

Great care must be exercised to guard against taking anything that will not be easily and completely digested.

Some vegetable substances contain an abundance of oxalic acid or the oxalates. This should be remembered, and such articles of diet should be avoided.

URATES.

Of these there are several forms: the amorphous, and the urates of lime, ammonia, soda, and potash. The ammonia and soda salts are crystalline and can be recognized as such under the microscope. All the urates are more or less colored in the urine, either brown or brownish-yellow, like uric acid.

FIG. 70.—URATE OF SODA, SHOWING SPIKED OR HEDGE-HOG CRYSTALS.

The urate of soda is generally in the form of round balls of considerable color, at other times they have fine, spike-like projections from their surface, when they are called the hedge-hog crystal; it is this form only that can be positively regarded as the urate of soda. Another form is described as round balls with fine lines radiating from the centre, but these crystals so closely resemble carbonate of lime that it is very hard, if not impossible, to distinguish them from each other. If deeply colored, they are probably urates; if white, carbonate of lime.

The urate of ammonia is seen as opaque, spherical masses, sometimes round or incompletely dumb-bell-shaped, often lying across each other at right angles, forming crosses; or aggregated together, resembling rosettes.

It is difficult, if not impossible, to distinguish the urate of soda from the urate of ammonia, unless the spiked balls or hedge-hog crystals

are distinctly marked. By their color it is impossible to separate one
from the other.

The addition or the formation of a free acid decomposes them, with
the formation of a soluble salt and later the deposition of uric-acid
crystals.

The urates may be distinguished from the phosphates upon the
slide by holding it, until quite warm, in the flame of an alcohol lamp
or Bunsen's burner. If the deposit is composed of urates, it will
disappear; but if made up of phosphates, it will become more
decided.

When the urates and phosphates are both present, the heat will
cause a marked diminution in the amount of sediment present, but
not a complete disappearance.

PHOSPHATES.

There are two classes: the *earthy* and *alkaline*. The former is the
only group of any practical importance in microscopic urinary ana-
lysis. The earthy phosphates are found in alkaline urine of low
density as a white and not very abundant precipitate. The urine,
when first voided, is sometimes cloudy from their presence, the re-
verse being the case when the urates are in abundance. In this way,
they may be differentiated at the time they are expelled.

When the urine is first voided, they are usually in the amorphous
state and only occur in this form with an alkaline reaction.

They are present when the food taken contains a large amount of
the carbonates, vegetable salts, the malic, tartaric, and citric acids;
continuous loss of sleep, nervous exhaustion from any cause, and ex-
cessive mental strains of all kinds, and in certain forms of dyspepsia,
which prevents the formation of sufficient acid.

This condition is often met with in connection with constant
brain workers, who habitually take but little exercise. Such persons
regularly pass turbid urine, due to the presence of the phosphates and
diminished acidity. Quantitative analysis of such samples will usually
show a diminution rather than an increase in these salts. From
this it would appear that their presence is due to diminished acidity
and not to an increase in the quantity of the phosphates.

Their perceptible presence, therefore, does not of necessity indicate
a diseased condition, but rather the taking of large quantities of the
above mineral substances, or a diminution in the acid production.
An abstinence from certain forms of diet, and plenty of out-door exer-
cise will often prove sufficient to cause their non-appearance and con-
sequently effect a cure.

The only special danger from the continuance of such a condition is the formation of a phosphatic calculus.

The *treatment* of this condition refers more to the regulation of the diet and exercise than to the administration of drugs.

The taking of mineral acids does not improve the condition, except in so far as it improves the general digestive and assimilative powers.

The *triple phosphates,* when slowly and perfectly crystallized, occur as white, transparent prisms, with bevelled edges. All grades of imperfect crystals are also met with. When rapidly crystallized, they are deposited in a variety of stellated, feathery forms. These can
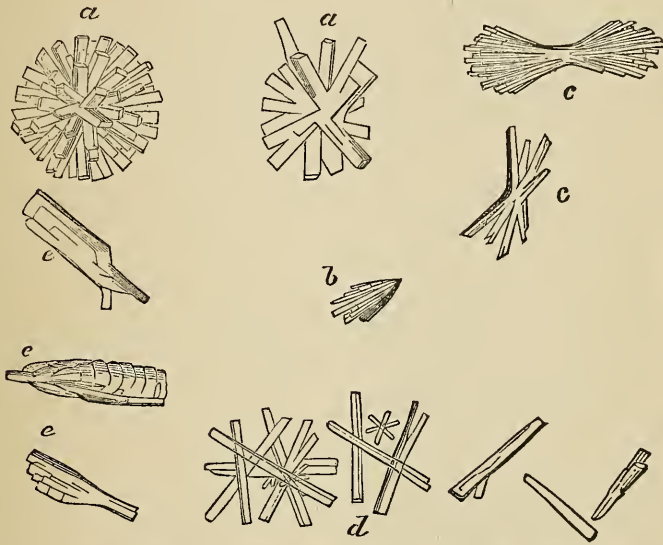
FIG. 71.—STELLAR PHOSPHATE OF LIME—CRYSTALLINE FORMS.

a, Stars; *b*, fans; *c*, bundles; *d*, rods; *e*, bottle-shaped.

easily be developed artificially by adding ammonia to urine. At one time this form was supposed to be due to the phosphates uniting with a very large quantity of ammonia. They occur as a white deposit or as a flocculent cloud resembling mucus, or as an iridescent scum on the surface of the urine; the two latter are the most frequent.

When the urine is faintly acid, boiling will cause quite a distinct cloud, which disappears instantly upon adding one minim of nitric acid.

The triple phosphates can occasionally be found in urine when first voided. This condition indicates retention of urine from some cause,

stone in the bladder, cystitis, and an alkaline decomposition before it is expelled.

They are, however, more frequently found in urine which has undergone alkaline fermentation outside the body; in fact, they are a product of this change.

They are occasionally found in conjunction with uric acid, urates, or oxalate of lime in the same sample and at the same time. In such cases, it is quite probable that the urine has not completely lost its acidity, and the previously formed acid deposits have not yet been completely liquefied.

As a rule, they are extra-vesical products, and therefore of no great clinical importance.

The *stellar phosphate of lime* is of rare occurrence and of no clinical importance. Under the *microscope* it appears in colorless crystals arranged in sheaves or rosettes. Its distinguishing features are its whiteness and arrangement with the clubbed formation of the periphery.

In this it differs from the rosettes of uric acid, which are pointed at the periphery, and which in the urine almost always have a deep yellow or brown color.

The stellar phosphate occasionally is developed just at the time the urine is changing from the acid to the alkaline reaction. But most frequently it seems to appear as an accidental formation in urine that has stood for a time in the laboratory.

It has no clinical significance.

MICROSCOPIC PIGMENTS.

Under this heading, blood, bile, urinary, and miscellaneous pigments will be considered.

Irregular bodies varying much in size are often found in examining urine, and they have considerable color, which is either yellow, brown, or red. Many of these particles are undoubtedly masses of desquamated epithelial cells or disintegrated corpuscular elements in which all evidence of a nucleus is absent; or they may be foreign bodies which have taken up the coloring matter of the urine or been colored before entering. They are, however, seldom met with, unless the urine contains blood or bile. From this it would appear reasonable to consider them as albuminous masses of varying shapes and sizes, which have attracted to themselves little particles of blood pigment or some of its derivatives, either melanin, urochrome of Thudichum, urobilin or purpurin of Prout, uroërythin of Heller, or indican. In other cases, biliverdin or bilirubin or some of their derivatives cause the color.

When carefully studied with a perfect and high-power lens and a strong light, they are without doubt very minute crystalline formations, probably derived from some of the normal or abnormal coloring matters present.

In cases of jaundice, all the desquamated epithelial cells and masses of protoplasm will be stained deep yellow.

These pigmentary bodies are of no special value, but often give rise in the minds of the students to the inquiry, Where do they come from and what do they indicate ?

It has been said that they were usually abundant in renal disease, and especially so in the lesions commonly included under the term chronic Bright's. The reverse, however, has been more often the case.

Many of the reddish flakes and delicately tinted scales resembling butterflies' wings are nothing more than little imperfections or hollows on the surface of the glass slides that have retained some of the red oxide of iron—used by the mechanic in polishing the glasses. They are often puzzling, and have caused many a mistake or new discovery.

CHAPTER X.

EPITHELIAL CELLS; SPERMATOZOA.

Epithelial Cells.—It is well known that there is great variety in the form of the epithelial elements found in the urine, some of which are] derived from the urinary tract, and others from the generative organs, while a smaller number may come from the air-passages, the mouth, or the skin. But, of all these, the variety known as flat or
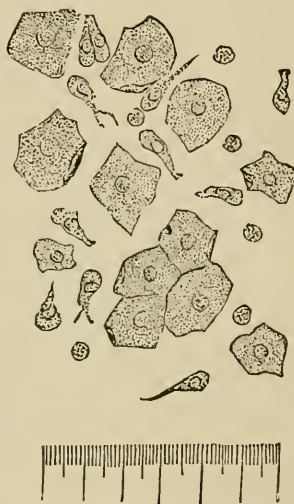
FIG. 72.—CELLS FOUND IN URINE.

Each division of the scale equals 0.0033 mm., or 3.3 μ—roughly, 3⅓ μ. The large flat cells average, probably, from 40 to 55 or 60 μ in their greatest diameter. Fifty cells, measured carefully by the author, averaged 49 μ in their greatest diameter, and 37 μ in the diameter at right angles with that one.

pavement epithelium, the tailed cells, and the small angular cells commonly called "renal," have given rise to the most discussion.

Naturally, epithelial cells from the urinary tract are found in either sex. On the other hand, the urine of the female is almost invariably said to contain a peculiar sort of large and angular cell that has been

regarded as peculiar to the sex. But all varieties, sizes, and forms of epithelial cells may come from the bladder, the ciliated form excepted. The structure of the bladder distinctly explains this, because it is divisible into three separate layers. The innermost or deepest is composed of several rows of small cells varying in size and shape, but usually cuboidal or rounded in outline. When these cells are shed rapidly they increase in size and have a more globular form, especially in catarrhal conditions or when the membrane is inflamed in any way. The intermediate plane is made up of a single or in part double layer of pyriform cells. Their tail-like prolongations are either single or double, but usually single, and fitted in between the epithelial cells of the deeper layer. Their rounded or outermost ends fit into depressions in the inferior face of the superficial cells.

Fig. 73.—Cells from Urine Removed Through an Abdominal Opening into the Bladder.

The third or outer layer is composed of a form of flattened cells called transitional. These cells are made up of large masses of protoplasm which usually appears to have two or more nuclei, but often this phenomenon is an optical illusion, and one at least of the apparent nuclei is produced by the fossa on their lower surface where it rests upon the underlying corpuscles. In cases of an ordinary catarrhal condition or inflammation, the epithelial membrane may be cast off in separate layers or with its three layers adhering together and appearing as such under the microscope. But a careful examination of the mucous membrane of the renal pelves, of the ureters, and of the vagina demonstrates that in all these regions the membrane is composed of three layers of cells similar to those found in the urine (Fig. 72 and Fig. 73) and from the bladder, ureters, and renal pelves (Fig. 74). Now, though the variety known as vaginal epithelial cells has been said to be the most common in the female, investigation shows that they are

quite as likely to come from the bladder, and even form the ureters or the pelves of the kidneys. There is another quite interesting point of medico-legal interest in connection with these cells, some alleging that they are always absent in the virgin. The author's attention was especially called to this subject when making a necropsy upon a female patient, aged eighteen, who had died twenty-four hours after a fracture of the skull. When the kidneys were examined they unexpectedly gave every macroscopic evidence of a chronic parenchymatous metamorphosis. The urine was desired for examination, to see if it contained evidence of the renal lesion, which it did in every particular. It was also found to contain an abundance of large flat cells identical with those commonly called vaginal, and single, and bifid-tailed cells also were abundant. In this case, the urine was not withdrawn through the urethra, but the bladder, which happened to be distended, was opened from the abdominal cavity, and its contents were withdrawn through a clean syringe. Excluding the vagina, and tracing the origin of these flat cells to the bladder, their frequency in the female and rarity in the male can be explained as follows: From the loose attachment of the bladder to the movable anterior wall of the vagina there is of necessity greater mobility in the female than in the male. The frequent motion and tendency to pouching of the trigonum vesicæ, and the more frequent over-distention in the female, naturally tend to excite a mild catarrh, which damages the epithelial cells, loosens their attachments, and easily accounts for their frequent and abundant desquamation. On the other hand, the firm attachments of the male bladder to the surrounding tissue, and its less mobility and distensibility, tends to hold the epithelial cells in their proper relations.

Another point of considerable interest in this connection is the dependence upon the tailed cells as diagnostic of pyelitis. One of Professor Satterthwaite's former students, Dr. Creedon, now of Globe Village, Mass., while working in the laboratory, prepared with great care specimens of the epithelial cells from the different portions of the urethra, bladder, ureters, pelves of the kidneys, and renal tubules. He made accurate measurements and also drawings of the cells removed from the various regions. The result of his research was that single and bifid-tailed epithelial cells were present throughout the mucous membrane of the urinary tract, from the meatus urinarius to the papillæ of the kidneys. He further found that the renal epithelial cells and those from the deeper layers of the urinary tract and from the uriniferous tubules of the kidneys also corresponded exactly in size and shape in all the specimens and in the different regions. Of course,

various sizes and shapes existed throughout. This careful observation was strong evidence in favor of the impossibility of locating with certainty the source of any given variety of epithelial cells when found in the urine. These experiments were made upon subjects in whom the membrane was free from any inflammatory process at the time of death. If the membrane was the seat of any inflammatory action, the rapid metamorphosis, subdivision, and desquamation of the cells would tend to make the similarity still greater. In the instance already cited, the tailed epithelium, both single and bifid, was abundant, but there was no evidence of pyelitis or any inflammatory condition of the urinary tract at the necropsy. There was, however, catarrh of the bladder. To establish more certainly the close similar-

FIG. 74.

a, Cells from the vagina; b, the six cells on the left came from the trigonum vesicæ, and the six to the right from the fundus of the bladder; c, cells from the ureter; d, cells from the renal pelvis.

ity in the shape and size of the epithelial cell in the various regions and layers, further examinations of the mucous tract were made, with the following result: A necropsy was made on another female, aged eighteen. Specimens were carefully prepared from the pelves of the kidneys, the ureters, the fundus and trigonum of the bladder, and the vagina. Drawings and measurements were made of the various kinds of cells from the different regions, also of the cells found in the urine taken from the bladder at the first necropsy. In all the different regions, and in both cases, the size and shape so closely corresponded that no apparent difference could be made out, as is well illustrated by the drawings. The various specimens were also measured and

20

the figures corresponded. The only variation that could be detected in the flat cells was a slight difference in size, those from the vagina and bladder being a little larger than those from the other two regions. The middle layer of the vagina contained cells that approached the spindle frm more than the poyramidal kind.

Renal epithelial cells have often been described as occurring free in the urine, and as being recognizable as such under the microscope, but the writer's opinion is that it is absolutely impossible to diagnosticate with certainty between renal cells and those of the deeper layer of the mucous membrane of the urinary tract. Either one might be mistaken for the other. Buccal epithelial cells may occasionally find their way into the urine, as when the receptacle for the urine served the purpose of a spittoon. They are, however, said to be distinguished from the vaginal cells by a more regular outline and by being larger. Specimens of these cells were prepared for comparison, but in size and shape they presented so many points in common that no marked difference could be drawn. Measurements of these cells gave the same results as those taken from the urinary tract and the vagina.

Ciliated epithelial cells are occasionally found in urine and may come from the air-passages through the sputa, but are more likely to come from the uterus or the Fallopian tubes in the female, and the ejaculatory ducts, vesiculæ seminales, or vas deferens in the male.

The results obtained by Dr. Creedon, and the above observations furnish additional proof of the untrustworthiness of the statement of Professor Ebstein in von Ziemssen's "Cyclopædia of Medicine," vol. XV., p. 574, that the occurrence of tailed epithelial cells in purulent urine was the most positive indication that the patient had pyelitis.

The conclusions deduced from this study are: that flat epithelial cells are found in the urine of females more frequently than in that of males; that they originate both in the vagina and in the bladder, probably more frequently in the bladder and the urinary tract; that they desquamate more frequently and in larger numbers from the female bladder on account of its loose attachment and greater mobility, and consequently are more frequent after the termination of virginity; that isolated angular "renal" cells cannot be distinguished from those of the third layer of epithelium at any point; and that no distinctive features can be ascribed to any cell or set of cells, by which its place of origin can be determined. But by a complete chemical and microscopic analysis, together with a complete history, very accurate results can be obtained.

SPERMATOZOA.

These microscopic bodies are frequently met with both in the male and female urine, but of the two, the latter is most likely to contain them.

They require a high power to distinctly bring out their outlines, although they can be recognized with a two-thirds objective.

Under favorable circumstances they are found to be composed of a head and tail united by an intermediate cylindrical body or middle piece. The head consists of a flattened ovoid mass, with a central depression on each side. They will appear broad or narrow depending upon the part presenting, whether the flat surface or the edge. The head is $\frac{1}{6000}$ of an inch (4.233 mmm.) long, and $\frac{1}{10000}$ of an inch (2.539 mmm.) thick, and is thickest at the attached end, which causes the free extremity to appear pointed. The tail is a tapering film projecting from the central piece, having a length of $\frac{1}{500}$ to $\frac{1}{400}$ of an inch (20 to 16 mm.).

They are sometimes with their fluid medium found in large quantities and from their albuminous nature will cause a cloud to appear in the urine upon the application of heat or the addition of nitric acid.

FIG. 75.—HUMAN SPERMATO-
ZOA.
1, In profile, the tail not represented; 2, viewed on the flat: *b*, head; *c*, middle piece; *d*, tail; *e*, end piece of tail (Quain's "Anatomy.")

They are only of practical importance in suspected cases of rape, and especially if the medico-legal side is in question.

They may be found in the mucus of the vagina after coitus, and have been known to retain their physiological activity for several days. Under favorable circumstances they may retain their power of activity for as long a period as ten or fourteen days. This probably in a measure accounts for the uncertainty of the date of impregnation and the exact duration of pregnancy.

They may be abstracted from soiled linen, by carefully soaking in a one-per-cent solution of sodium chloride for fifteen or twenty minutes.

When found in the urine, they are generally inactive.

In one instance they were found at the necropsy in the cavity of the uterus of a young woman who had committed suicide by jumping from the third-story window.

CHAPTER XI.

VEGETABLE ORGANISMS; FUNGI.

VEGETABLE ORGANISMS.

(*a*) *Sphero-bacteria* or *micrococci* are minute spherical particles of protoplasm not more than $\frac{1}{25000}$ of an inch (1 mmm.) in diameter. Their protoplasm is believed to consist of an outer envelope and cell contents; the cell wall closely resembling cellulose. They resist the action of alkalies, acids, heat, and cold to a wonderful degree. They refract light, and are decidedly colored by some reagents.

These bodies, like all bacteria and bacilli, multiply by transvere fission. In this way they form, chains, clumps, or large globular masses.
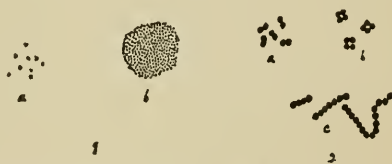
Fig. 76.—Sphero-Bacteria (Genus Micrococcus). × 700.

1. *a*, Single; *b*, zooglœa. 2. *a*, in pairs (diplococcus forms); *b*, in tetrads; *c*, in chains (sometimes designated a streptococcus. (Delafield and Prudden, "|Handbook of Pathological Anatomy and Histology.")

When packed together in these large masses they form what are called by some zooglœæ; and it is supposed that they are held together by a delicate film of intercellular substance. They do not grow into rods or filaments, like other forms, and according to Cohn have no independent power of locomotion, thus differing from the bacteria proper and the bacilli.

Under the microscope and in urine they appear as minute highly refracting dots, and if suspended in the fluid show an active Brownian movement. When single and isolated it is hard to distinguish them from minute fat droplets or granules of protoplasm. But they can be distinguished when aggregated together by their uniform size, and

by being disposed at equal distances from one another. Fortunately they are frequently found in rows, pairs or large accumulations.

If dividing rapidly, they often appear dumb-bell like in shape, and have a to-and-fro movement. When dividing more slowly, they are seen forming rows or chains of four, six, or more linked together. Under favorable circumstances, they frequently form the globular masses united together by an intercellular substance.

Occasionally a transverse and longitudinal fission takes place at the same time, and groups of four-celled " sarcinæ forms " are produced.

All these different forms may be found in a single sample.

The globular masses are very common in urine, and it is sometimes difficult, if not impossible, to say whether these masses are groups of micrococci, degenerated epithelial corpuscles, or masses of transformed protoplasm. It often requires a staining reagent and an unusually high power to solve the question, but with them it is not difficult, except when the cells are single.

Micrococci may be so abundant or develop so rapidly that urine even at first, or a clear sample will soon be opaque, and in some cases white dots as large as the head of a pin can be recognized with the unaided eye. They then usually become stained by the absorption of the coloring matter present in the urine.

They require for their growth a nitrogenous pabulum, oxygen, moderate temperature, moisture, and a faintly acid or alkaline medium.

(*b*) The *sarcina* is another microscopic vegetable organism of the sphero-bacteria type and is one of the lowest orders of saccharomycetes. They were first described by Goodsir in 1842.

There are two principal varieties described, the sarcina ventriculi and s. urinæ. Both are found in the urine. Still other varieties have been mentioned.

The sarcina ventriculi is described as coming from the stomach in connection with a number of diseases, and with the vomited matter occasionally fall into the urine.

The sarcina urinæ is probably developed outside of the sample and accidentally gets into it. In either case, the sarcina appear under the microscope as little collections of sphero-bacteria arranged in groups of four, sixteen, sixty-four, and so forth, which have a tendency to divide or split off from the mother mass in the same numerical order.

They differ from similar micrococci formations in this, that the spherules are larger, have a diameter of $\frac{1}{16000}$ of an inch (1.587 mmm.), in their peculiar arrangement and division.

The only difference between the s. ventriculi and s. urinæ is a slight variation in size, the spherules of the former being a little larger; the diameter of the spherules of the s. urinæ coming between those of the s. ventriculi and the micrococci proper.

The author has never found either of the above forms, and Prof. Satterthwaite, who has had a very large experience in urinary analysis, also informs him that he has never met with them.

(c) *Micro-bacteria* or *Simple Bacteria.*—Under this title many forms of organisms have been described, but of late the unqualified term has become a distinct order by itself, so that now the term is empirically limited to rod-shaped bacteria, in which the length and breadth have a certain relation to each other. A simple bacterium must be *just* one half as broad as it is long. Their length is $\frac{1}{10000}$ of an inch (2.539 mmm.), and their breadth $\frac{1}{20000}$ of an inch (1.269 mmm.).

This variety is the one most frequently found in all samples of

FIG. 77.—MICRO-BACTERIA (GENUS BACTERIUM).

1, Bacterium termo; 2, bacterium lineola. Specimens stained with fuchsin. × 600. (Delafield and Prudden, " Handbook of Pathological Anatomy and Histology.")

urine. It may be well to observe here that they will vary much in size, notwithstanding the above arbitrary rule.

They are often quite abundant and render the urine cloudy by their presence in the same way as the micrococci. They may be found immediately after drawing the urine with a catheter; this, however, is exceedingly rare except when the urine is alkaline before it is voided or in connection with cystitis and pyelitis.

In one case in which there was no cystitis or pyelitis, and in which the urine was acid, it persistently contained bacteria in abundance when first voided or was withdrawn by a carbolized catheter. The patient was suffering from an atrophic form of diffuse nephritis and the urine was heavily loaded with albumin.

As a rule, an hour or two elapses after voiding before they make their appearance. If the urine is free from epithelial cells or albuminous elements, it will often stand exposed to air for days without any bacteria being found in it. The rapidity and the abundance of their formation appears to be influenced by the amount of albumin primarily in the sample.

(*d*) *Vibriones*.—These are organisms of the micro-bacteria type, and are found in the urine at any time after it has been expelled from the bladder. They vary considerably both in size and shape, and are found most frequently and abundantly when decomposition has become established.

When viewed under the microscope, they are about one-three-thousandth of an inch (8.466 mmm.) long, and quite broad compared with other forms. They are always in motion, and are propelled by a spiral or twisting motion; sometimes they revolve upon their own axis at a tremendous rate of speed. It is quite evident that they are not dependent upon the fluid for this motion, for they move as rapidly against the current as with it. This movement of the whole organism differs from the Brownian movement, which consists in a constant motion of the granular particles composing the mass of protoplasm.

(*e*) *Leptothrix*.—This is a micro-bacterium or vegetable organism that appears under the microscope as a minute filamentous body having considerable length and but little breadth. It is usually found in scrapings from the buccal cavity and in the contents of carious teeth. It was at one time supposed to be in some way connected with, if no the cause of, certain forms of aphthous sore mouth, but it has since been found to be a normal habitant of the buccal cavity. It occasionally finds its way into the urine.

FIG. 78. — LEPTOTHRIX BUCCALIS WITH MICRO-COCCUS COLONIES FROM THE MOUTH OF A HEALTHY PERSON, STAINED WITH GENTIAN VIOLET. × 600. (Delafield and Prudden, "Handbook of Pathological Anatomy and Histology.")

(*f*) *Desmo-bacterium* is the one exciting considerable interest in reference to the causation of certain infectious and contagious diseases, and requires a few words.

A typical *bacillus* is a rod-shaped body, the length of which is more than twice the breadth. In general, its length is about one-ten-thousandth of an inch (2.539 mmm.), and the breadth one-eighteen-thousandth of an inch (1.411 mmm.) or less. The length and breadth vary with the variety.

The two micro-organisms which are most likely to be found in the urine are the *bacillus tuberculosis* and the *gonococcus*, the former reaching the urine through the medium of the sputum, or in cases in which there is a tubercular lesion of the genito-urinary tract the latter would be swept in during micturition.

The different varieties of bacilli can only be distinguished by their minute variations in size and shape and their behavior with certain

aniline dyes, or by cultivation. The latter, however, is wholly im-
practicable for general use.

It is not at all likely that their detection in the urine will ever be
necessary or will yield any very satisfactory results if attempted.

Bacteria in general are said to be plain, jointed, or mono-tailed,
depending upon the stage and rapidity with which they are dividing.
This, however, according to the present classification, would be more
applicable to vibriones, leptothrix, and bacilli, but not to the simple
bacterium.

At this point, it may be said that in highly putrescent fluids all
forms of bacteria multiply rapidly and are apt to be undersized, while
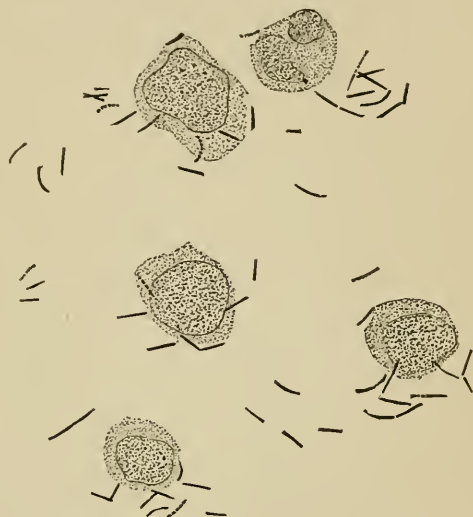
FIG. 79.—BACILLUS TUBERCULOSIS. × about 800.
(Delafield and Prudden, " Handbook of Pathological Anatomy and Histology.")

in less putrescent fluids they divide more slowly, are more perfectly
formed, and larger than the average.

The volumetric bulk, on the contrary, will be greatest in the first
instance, least in the latter, while the vitality will be least in the former,
and greater in the latter case.

Up to the present time, it is a mooted question whether bacteria
cause fermentation and putrefaction or are a concomitant product of
this change. Pasteur and believers in his germ theories are strong
in their belief that these micro-organisms must be introduced into the
substance before new micro-organisms can be developed.

The opponents of these theories believe that they are developed as
the result of fermentation.

The germ theorists claim that all diseases have a separate and distinct bacillus or micro-organism for each given disease. In some instances, this at first seems quite probable; but if we observe that, as a rule, the germ, which was supposed to be essential to some particular disease, is found in reality in every human individual without producing the malady, it is not surprising that we should be sceptical on the subject. In almost all the instances where the local seat of the disease can be easily reached, careful research reveals in healthy subjects precisely the same micro-organisms. This raises the question, might not this prove true in the more deeply seated diseases, provided as careful a search could be made in perfectly sound subjects ? They may not be either the cause or the products of the disease, but intermediate agents between the true cause and the effect.

These micro-organisms may yet be found to be important factors in producing disease. It has been a firm conviction for a long time that they bore the same relation to a disease that a hod-carrier does to the erection of a wall or building. He neither produces the bricks and mortar, prepares the foundation, nor lays the wall. So with the bacillus. It has not been proven to produce the poison, to prepare the system for its reception, nor institute the building up of the disease.

It appears, therefore, that these four conditions must be considered in every abnormal process. The *preparation* of the system for the reception of the *poison*, the *means* of *transportation* of the poison, and the *builder* of the disease. Thus far, only one of the four has been mastered, which is the laying of the foundation; the cause and medium of transportation, and the elements which set the poison in motion remain as yet absolutely an unsettled question.

The foundation of every disease is unquestionably laid by dissipation and everything which tends to diminish a perfect physiological standard, namely, bad air, bad food, and bad hygienic surroundings, as well as over-work, either physical or mental or both.

The part attributable to the micro-organisms is rather that of the hod-carrier depositing the poison upon suitable ground for further growth, development, and destruction. There is no doubt in reference to time intervening between the introduction of the poison and the result.

It may be that the poison attaches itself to these bacilli ; and as they increase in number it also becomes more virulent, until finally there is enough developed to produce a given result. Or, it may be that, by their rapid multiplication, with their active movements, they spread out until a weak point is reached and the poison thus gains access to the system.

Accepting this view of the subject, the bacilli are as important as the actual cause of the disease, and perhaps even more so.

Antiseptic treatment is still called for and possibly may be found of still greater service. The efficacy of antiseptics now appears to be in preventing the activity of their movements and in controlling their growth and development which prevents the development and spread of the poison.

If these micro-organisms were the absolute cause of the disease and acted as a poison, it would seem as if they ought in every instance, and on every subject to work alike, the same as acids and alkalies, but the quantity introduced appears to have an inverse ratio to the result attained. This is often exemplified in purely contagious diseases, where a little poison from a very mild case will produce in the second person a very intense attack and *vice versa*.

Again, it does not seem possible to find and appreciate enough different varieties to account for all the known diseases.

FIG. 80.—DESMO-BACTERIA (GENUS BACILLUS). BACILLUS ANTHRACIS, FROM SPLEEN OF MOUSE INOCULATED WITH THE BACILLUS. SPECIMEN STAINED WITH METHYLEN BLUE. × 600.

(Delafield and Prudden, " Handbook of Pathological Anatomy and Histology.")

In the case of the modified anthrax virus it was found that protective inoculation killed a larger percentage in protecting the remainder than if the animals were left to the original disease, which was poor encouragement for the stock raisers. This also tends to substantiate the fact that slow and perfect development increases the destructive power.

Unless better results can be secured in the diseases affecting the human race little good can be hoped for from a modified virus and protective inoculation.

The differences in the reaction of the bacilli with different staining methods may be explained by the variation in their age and method of production. It is a well-known fact to every one familiar with histological and pathological work, that all forms of organic protoplasm stain differently at different stages of their development, and as a result of the various retrograde changes which they undergo. Why is it not just as reasonable to attribute the different reactions of different stain-

ing reagents to such changes as it is when they occur in the centre and periphery of an epithelial carcinoma? No one seems to have thought it necessary to attribute different causes to these two points.

FUNGI.

There are two important forms found in connection with urinary analysis—the mould and the yeast or sugar fungi.

(*a*) The *penicillium glaucum* is that variety of fungus which forms mildew. It occurs quite frequently in urine that is slightly acid or commencing to turn alkaline. It may appear with or without the presence of albumin or sugar. It is composed of three parts: the mycelium which is made up of an interlacing network of sporules;
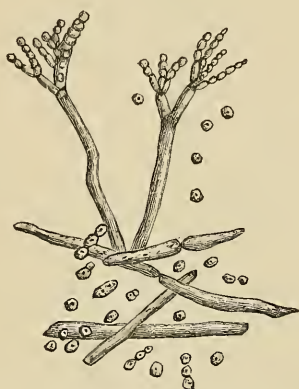
FIG. 81.—PENICILLIUM GLAUCUM SHOWING MYCELIUM, STIPES, AND THALLI.

the stipes or stems are surmounted by their thalli and grow upwards from the mycelium, and from the branching tufts the sporules are constantly being desquamated.

What is most commonly seen under the microscope is the single sporule, and occasionally a thallus and still more infrequently the mycelium.

The sporules are usually oval, considerably larger than a pus-corpuscle. They have quite a clear cell contents with a distinct nucleus. In focussing down upon them, they are found to have greater depth than pus or blood-corpuscles with which they are sometimes confounded. Two, three, or more are often found joined together with an occasional branching thallus. By the latter they are positively distinguished from pus or blood, and this also distinguishes them from yeast fungi.

(*b*) *Torula cerevisiæ*, or yeast fungus. When yeast is placed in a

fermentable fluid, its cells multiply not by fusion, as in lower algæ, but by the budding fourth of young cells from the parietes of a pre-existing spore. In the course of a short space of time, one cell will have developed into three, four or five more complete cells which remain in continuity until the plant stops growing, but separate and return to the parent form if the fermenting process is checked or arrested. If the process continues to full development, a mycelium will be formed, from which stipes shoot upward and are surmounted by a spherical thallus. It is the bursting of the thalli and the setting free of the sporules that causes their appearance in the urine.

(c) The *Saccharomyces cerevisiæ*, or *S. urinæ*, is almost identical, if
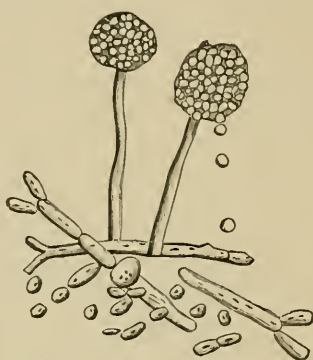
Fig. 82.—Representing Yeast and Sugar Fungus. Showing Mycelium, Stipes, and Thalli.

not isomeric with the former. This plant grows in the same way as the torula, by a process of budding. The cells are usually round and have a thin investing membrane which incloses a finely granular substance, containing one or two transparent spots called vacuoles. These spots are little cavities filled with a clear fluid. The cells usually are single and about $\frac{1}{300}$ of an inch (12 mm.) in diameter. The majority are isolated, but occasionally two or more are joined, forming moniliform chains.

It is only by finding a stem and its attached thallus that we can be positively sure that the sporules are of the yeast or sugar variety, and not due to the penicillium glaucum.

CHAPTER XII.

CASTS.

There are two principal types of casts: the blood and the hyaline; in connection with the latter, there is a large modification as may be seen by a single glance at the following table:

		Small.	*Large.*
CASTS.	1. Blood...............	....	....
	2. Hyaline..........	....	....
	3. Epithelial.........	....	....
	4. Nucleated.........	....	....
	5. Finely granular...	....	....
	6. Coarsely granular.	....	....
	7. Fatty........ ...	.. ..	.. ..
	8. Tubular..........	....	....:.................
	9. Cork screw.......	....	....

The *blood cast* is simple, and easily understood. It is produced by an exudation of all the constituents of the blood, and a matting together and entanglement of the blood-corpuscles by fibrin elements in the lumen of the uriniferous tubules. They are discharged from the tubes in masses, representing perfect casts of the portion of the kidney from which they have escaped. They are found in the urine as little plugs of blood-corpuscles with parallel sides and rounded ends. This variety is only met with in acute congestion, hemorrhagic infarctions, hæmaturia, acute diffuse nephritis, and acute exacerbations of the chronic diffuse nephritis. The presence of blood casts in the urine is the only *positive evidence* of *hemorrhage* from the kidneys. Their presence alone does not indicate organic renal disease. Some call the hyaline, with a number of blood-corpuscles attached to them, blood casts, but this is erroneous. Blood casts are not common.

The *hyaline cast* is not so thoroughly understood, but it is generally believed that a peculiar fibrinous substance is thrown out of the blood into the uriniferous tubules, and when discharged independent of the epithelial cells, it is known as a hyaline cast, but with attached epithelial corpuscles, in various stages of retrograde change, the various forms tabulated are produced.

A single cast of this variety may be found in urine without indi-
cating any renal lesion. But their continuance in any appreciable
number is always an indication of some retrograde change.

FIG. 83.—CASTS. × 500.

1, Small blood.

2, Small hyaline.

3, Small epithelial.

4, Large blood.
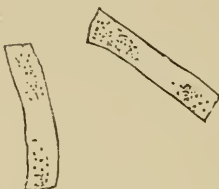
5, Large hyaline.

6, Large epithelial.

7, Small nucleated.

8, Finely granular.

9, Coarsely granular.

By an *epithelial cast* is meant one in which the epithelial cor-
puscles are attached to, or implanted, in this hyaline plug, having
been separated from the basement membrane, and still retaining the
appearance of renal epithelial cells. Casts of this kind are usually
found in the acute parenchymatous metamorphosis of the kidneys,
and in the acute diffuse nephritis, or in connection with acute exacer-
bations.

The *nucleated cast* is one, in which the protoplasm of the epithelial cells has been obliterated, and only the nuclei can be recognized

FIG. 81.—CASTS. × 500.

10, Large nucleated.   11, Finely granular.   12, Coarsely granular.

13, Small fatty.   14, Small corkscrew.   15, Small tubular.

16, Large fatty.   17, Large corkscrew.   18, Large tubular.
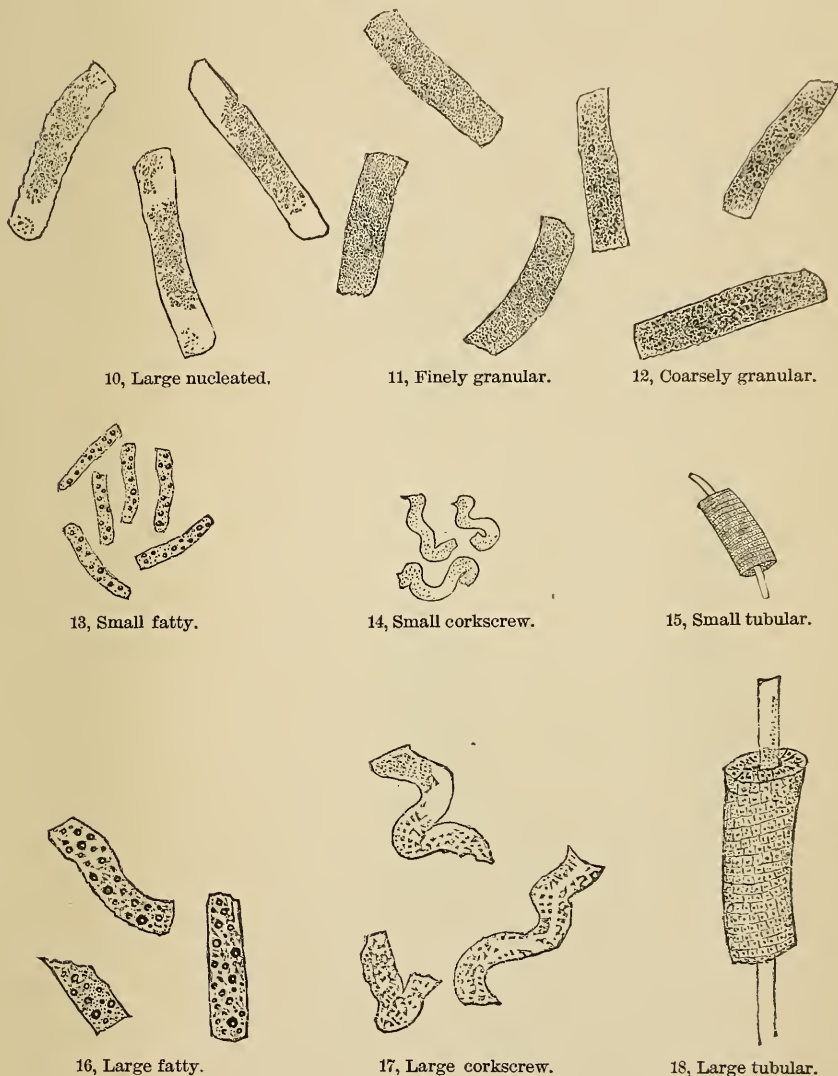
as they adhere to or are implanted in the hyaline substance. The inability to recognize the protoplasm is caused by the cells becoming

infiltrated with fine particles of effete material and the imbibition of an albuminous fluid until everything is indistinct but the nucleus.

This form of cast is met with in the acute parenchymatous metamorphosis of the kidneys, in diffuse lesions, and in acute exacerbations; it indicates a still greater retrograde change in the epithelial cells.

FIG. 85.—CASTS × 1,200.

1, Hyaline.   2, Epithelial.   3, Nucleated.
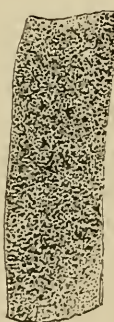
4, Finely granular.   5, Coarsely granular.   6, Fatty cast.
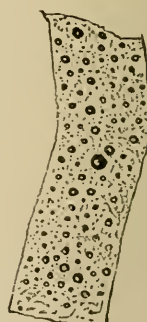
The *finely granular cast* is one in which the epithelial cells are not only cloudy, but are also infiltrated with fine granular particles, some of which are oil-globules of minute size, and others granular detritus probably from incomplete products of tissue metamorphosis drawn from the blood, and in part from the further destruction of the epithelial protoplasm itself.

This form of cast represents a still greater destructive change, and is met with in a well-established acute lesion, or in the commencement of a chronic lesion.

The *coarsely granular cast* is simply one representing a more advanced degree of the former process, with more abundant and larger fat droplets, and a still greater destruction of the epithelial protoplasm.

This form is met with at the end of an acute lesion, but more frequently indicates a chronic parenchymatous metamorphosis or a diffuse lesion of the renal glands.

The *fatty cast* is one in which the metamorphotic process has almost, if not completely, destroyed the protoplasm of the epithelial corpuscle, which has been replaced by fat droplets of varying sizes, which are easily recognizable. The cast may have a large or small diameter, but the former is the more common.

This form indicates an advanced stage of the chronic parenchymatous metamorphosis or a chronic diffuse lesion of the kidneys.

The *tubular cast* is a rare variety, and is formed by a plug of hyaline matter in the lumen of the uriniferous tubule and a thin ensheathing layer of the same material behind the epithelial cells; in this manner the corpuscular elements are detached from the basement membrane and discharged. They appear under the microscope as a perfect ring of epithelial elements. Occasionally the central plug will be observed protruding from one or the other extremity.

This variety might be considered as a curiosity.

The *corkscrew cast* is produced by a twisting of the body of the cast upon its own axis, so that it resembles the spiral of a corkscrew. This opinion is based upon numerous sections of the kidneys that show this peculiar arrangement in the straight tubules, some of which have the casts still lodged in them.

Some believe that all forms of casts (the blood, hyaline, and tubular excepted) can be, and are frequently formed by the transformation, desquamation, and matting together of the epithelial cells without the aid or the presence of this fibrinous or hyaline material. This may be the case in a few instances, but in the vast majority the hyaline material forms the basis of all casts. In either case the microscopic appearances are the same.

The peculiar arrangement of the tubular cast appears to denote that the protoplasm is clogged by the hyaline material, which cuts off the nutritive supply, prevents the free escape of the effete material, and enables the substances, which should pass through, to push the cells from their attachment to the underlying basement substance.

21

This view of the situation distinctly indicates the necessity of keeping the tubules well washed out in all forms of renal disease, in which there is a tendency to the formation of casts.

It is the belief of some that the hyaline material undergoes degeneration, and in this way they explain the various forms of granular casts. A close examination, however, of a hyaline cast, which appears to be a little granular, will almost always, with a good high-power lens, show the incomplete and faint outline of what once was an epithelial cell. This tends to sustain the former view, and to disprove the latter.

The *waxy cast* of some writers is not included in this classification as its existence is extremely doubtful.

It occasionally happens that the various crystals of the urine adhere to these hyaline plugs, or to a cast, and these might be termed crystal casts. They are, however, more likely to be seen in sections made from the kidneys than in the urine.

The distinguishing character of all casts is that they have uniformly parallel sides, and usually at least one rounded end, occasionally the other end is broken at a right angle, or a little irregularly, but they never terminate in imperceptible lines, as is the case with bands or streaks of mucus. Casts and strings of mucus are often confounded; but by remembering the above-stated facts, the one should never be mistaken for the other. If the observer will compare the diagrams of casts as seen in the books with specimens of ropy mucus from the bladder, the difference is at once apparent.

Casts are very important aids in diagnosis. They are found in acute and chronic parenchymatous metamorphosis of the kidneys, in acute diffuse nephritis, and in the chronic diffuse varieties. They are rarely found in the sclerotic, gouty, and waxy kidneys when uncomplicated.

Small casts of the hyaline, epithelial, nuclear, and finely granular variety are found in the acute lesions, and in the early stage of the more chronic forms. Large hyaline, coarsely granular, and fatty casts indicate an advanced lesion.

By a careful microscopic study of the size and the amount of retrograde metamorphosis in the casts, a very accurate knowledge of the extent of retrograde change in the uriniferous tubules will be obtained. In this way an accurate prognosis can be given.

PRESERVING CASTS.

It is difficult to preserve casts, more especially if alkaline fermentation has occurred. Various methods have been proposed. The three which have been found most serviceable are:

First, by adding a 2% solution of salicylic acid to the sample containing the casts. In one case, they were well preserved eighteen months after the acid had been added.

A second method, or that employed by Dr. G. R. Elliott in the laboratory of the New York Post-Graduate Medical School, has been found even better than the former. It is as follows: *First,* allow fresh urine to settle in a conical glass for twenty-four hours. *Second,* decant, *i. e.,* pour off the supernatant fluid. *Third,* add to the residue eight ounces of pure water and pour this mixture into a long and narrow graduate. *Fourth,* add to the solution number three one

FIG. 86.—CONICAL RECEPTACLE FOR COLLECTING SEDIMENT.

drachm of a saturated alcoholic solution of picric acid and mix. *Fifth,* allow solution number four to stand four days. *Sixth,* decant the supernatant fluid and wash the residue by adding pure water and allow the mixture to stand twenty-four hours. *Seventh,* decant and add to the residue one ounce each of glycerin and pure water.

This plan has been found quite satisfactory, the casts retaining their microscopic features quite distinctly for many months. When prepared in this way, they are quite serviceable for class demonstration. The only objection is that they are misguiding, being much plainer than when ordinarily seen in urine.

Another very good way to keep them a few days is to add half a drachm of an alcoholic solution of eosin. This not only perserves the casts, but it stains all the organic matter, and consequently renders the casts more plainly visible.

The great objection to staining casts is that it may not always be convenient to do so, and unless the examiner becomes perfectly familiar with them in their natural medium, it may lead to gross errors.

CHAPTER XIII.

SEDIMENTS OF DOUBTFUL ORIGIN; LIME CARBONATE; FATTY MATTERS; CHOLESTERIN; CYSTIN; LEUCIN; TYROSIN; XANTHIN.

SEDIMENTS OF DOUBTFUL IMPORTANCE.

There are a number of substances occasionally found in the urine, some of which are indicative of a morbid condition of the body, while others are purely of extraneous origin. But from the frequency with which some of them are found in microscopic work, it is necessary to speak of them, and it is also absolutely essential to be thoroughly familiar with their appearances. Many samples are found to contain more extraneous matter than substances of intrinsic importance, and unless this point be fully appreciated, many a gross error may easily be made.

LIME CARBONATE.

This substance is rarely, if ever, found in the human urine, although it is one of the constituents of the body. It is always present in large quantities, however, in urine taken from horses. Lime carbonate from the lower animals occurs as spherical masses with fine lines radiating from the centre; it has the same characteristics when found in the human urine.

Some of the crystals of the urate of ammonium are said to closely resemble those of lime carbonate, and the question arises which of the two are present in the urine of the human species.

The carbonate of lime is recognized by its effervescing when brought in contact with acetic acid.

If urine becomes alkaline from the presence of ammonium carbonate, lime carbonate may be precipitated in the amorphous state along with the earthy phosphates, but occasionally it assumes the crystalline form.

The lime carbonate is found as an ingredient of urinary calculi when developed in the human system, but this form of calculus is

about as infrequent as the crystals themselves. Practically speaking, this salt may be said never to occur in the urine of the human being, while it is almost constantly present in the herbivora.

FATTY MATTERS.

Fat may occur in the urine as spherical droplets or globules of a high refracting power or in the form of acicular crystals.

The characteristic microscopic appearance of fat globules is their very high refracting power. They may present themselves as minute droplets or as large and easily recognized globules. They have a circular form and sharply-defined marginal outline. They may or may not have an amber color, and always act as double convex lenses, the result of which is that they have a very bright centre and a dark and rather broad peripheral band, which sometimes is almost black. As the lens of the instrument is drawn away from the globule, its centre increases in brightness and the margin becomes darker until finally it is lost.

Fat may occur in the urine free and in large quantities, in the disease called chyluria, and occasionally from eating too much oily food. It also occurs free, but in small quantities, in renal lesions in which there is disintegration of the epithelial cells of the uriniferous tubules, or it may be imbedded in the protoplasm of a desquamated cell or in the form of a fatty cast.

Free oil globules are quite common in the urine from the fact that patients do not sufficiently realize the necessity of using perfectly clean bottles. It is often collected in bottles which have previously contained hair-oil, etc., and in this way much of the fat found in the urine may be accounted for.

Fat crystals are occasionally found, either in the form of a stearate or palmate. The two varieties have nearly the same form, i. e., fine needle-like crystals. These and the crystals of leucin somewhat resemble each other. The fat crystals, however, are produced directly from the oil itself, while the leucin is dependent upon an impaired hepatic digestion and an incomplete proteid metabolism.

The microscopic mirror and the fat globule, which acts as a double convex lens, will often reproduce some object within the rays of reflection, such as the window, so that it is distinctly visible to the examining eye. The image appears to be located in the fat globule.

CHOLESTERIN.

These crystals are occasionally found in the urine in attacks of jaundice and in connection with chronic suppurative nephritis.

Roberts records one case only, and quotes another by Murchison. The author has also seen one case in which there was an abundance of cholesterin in the urine, and the necropsy revealed a suppurative nephritis.

The crystals are always easy of recognition, composed, as they are, of thin, white and transparent plates which have a square piece missing at one corner. They often pile themselves up in masses, the notched corner of one plate always lying near the notched corner of the opposed crystal.

The tests for cholesterin are: (1) Add to some crystals strong sulphuric acid with a little iodine or zinc chloride; they acquire a tint which varies from greenish-blue to violet. (2) Put a drop of concentrated nitric acid on a crystal in a porcelain capsule, and evaporate to dryness at a gentle heat; touch the residue with a drop of ammonia. A deep-red color is produced. (3) Rub up cholesterin with strong sulphuric acid, and add chloroform. A solution varying in color from blood-red to purple is produced, which, after changing successively into violet, blue, and green, finally disappears.

CYSTIN.

This substance is rarely met with in the urine, and is only of importance from the fact that it is considered as an originator of calculi.
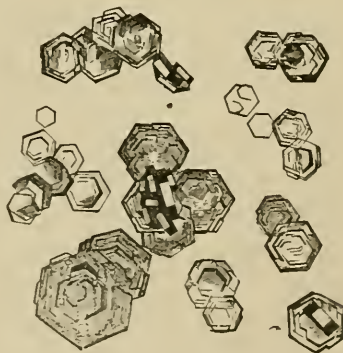
FIG. 87.—CYSTIN

It is also said to be peculiar from its presence in the urine of successive generations. It is a highly sulphurous body containing twenty-

six per cent of sulphur, and is apparently closely allied to taurin, although nothing is known of its origin.

Under the microscope, it is seen to be composed of hexagonal crystals which often form aggregated masses, which may become the nucleus of a calculus. When rapidly crystallized from an ammoniacal solution, six-sided tablets and square prisms are formed. The former closely resemble uric acid. Cystin crystals are distinguished from uric acid by being soluble in ammonia, from which they form perfect crystals upon evaporation; but the uric acid forms ammonia urates, and is not recrystallized. The murexide reaction is not obtained with cystin.

LEUCIN.

This is one of the intermediate products resulting from the transformation of the proteids. From it urea is supposed to be produced, which is the final product of a perfect and complete metabolism.
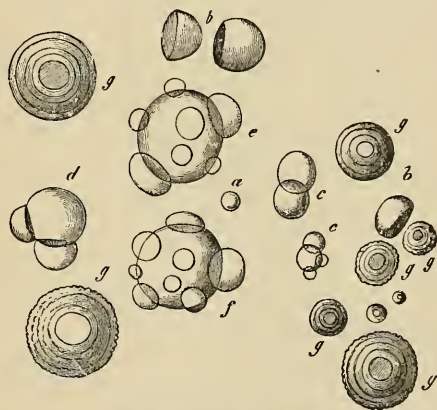
FIG. 88.—LEUCIN SPHERES.

The microscopic test for this substance is quite uncertain, for the reason that many other substances have the same appearance, and consequently errors are constantly being made by mistaking them for it, and *vice versa*.

Unless the patient is suffering from some of the diseases previously mentioned (p. 268), the diagnosis of its presence is extremely doubtful.

It usually appears as highly refracting spheres, often tinged yellow, and might easily be mistaken for fat globules. Leucin also forms slender white glistening plates, or occurs in very thin plates grouped

in a radiating fashion.   They differ from the urates, which are not strongly refracting bodies.   The chemical tests have been given on p. 268.

TYROSIN.

The statements regarding the former substance are equally applicable to this, the two always being together, and have the same causes.

Tyrosin crystallizes in delicate needle-like forms, which often arrange themselves in sheaves or bundles, and appear as such under

FIG. 89.—TYROSIN.

the microscope.   They may be mistaken for the acicular crystals of the fats, but can be distinguished by the chemical tests given on p. 269.

XANTHIN.

Whetstone crystals of this substance have been described as occur-
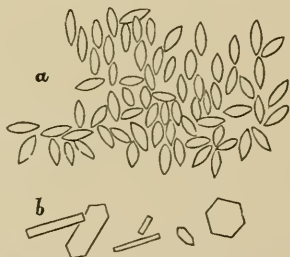
No. 90.—WHETSTONE-SHAPED CRYSTALS OF XANTHIN.
b, Crystals formed after adding hydrochloric acid.   (Neubauer and Vogel.)

ring in the urine, but there appears to be some doubt in relation to

them, as they are so closely resembled by some of the uric acid crystals. The question naturally arises, are they not the white crystals
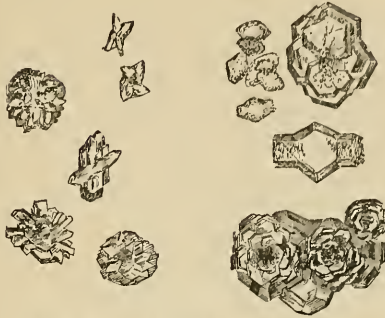
Fig. 91.—Hydrochlorate of xanthin.

of uric acid which have been mistaken for the xanthin? Hydrochlorate of xanthin is more diagnostic in its crystalline form.

FOREIGN MATTER.

There are quite a number of extraneous substances, wholly foreign to the urine, with which the examiner should make himself thoroughly familiar. The reasons for this are that these substances almost invariably get into the urine and have often led to serious mistakes in diagnosis.

(a) *Human hair* appears under the microscope as large shafts of considerable length, and varying in color. Human hair has a longitudinal striation and at places the centre is darker and more granular than the periphery. The distal extremity is striated and granular, but near the root distinct interlacing lines are readily seen which indicate the outline of the cell covering.

(b) *Cat's hairs.*—These also are quite common in urine and differ from the former in this, that their centre is very dark in color, surrounded by a narrow transparent band, and on the surface the cell markings are even more distinct than on human hairs.

(c) *Muscle fibres.*—Occasionally we find meat fibres in the urine, and they are generally of the striated variety. Owing to a partial disintegration, the transverse and longitudinal striations are only faintly marked, but are sufficiently distinct to be recognized as muscle tissue.

(d) *Oil-globules.*—Fat is not infrequently found as a foreign element in urine (see p. 325).

(e) *Air-bubbles.*—These are found in almost every sample mounted.

They are usually spherical, but may assume almost any form. They have a bright and vacant centre with a dark peripheral margin, in the centre of which there is a very narrow white circle.

(*f*) *Feathers or fragments* of them coming from the bedding or dust brushes are frequently found. If a single shaft is examined, it is knobbed and resembles a series of fish-hooks broken off at their bases and joined point to base. In the feather, the point is attached to the common stalk and the base is the free extremity. The fragment of a stem and a few attached branches may occasionally be seen under the microscope.

(*g*) *Cotton fibres* appear at first as small fibres with nearly parallel outlines and longitudinal striations, but by following along its course it will be found to twist upon itself so that the right border will
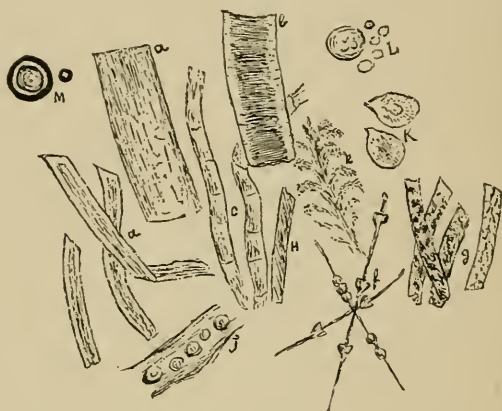
FIG. 92.

a, Human hair; *b*, cat's hair; *c*, flax fibre; *d*, cotton fibre; *e*, feather; *f*, knotted portion of shaft; *g*, wool fibre; *h*, silk fibre; *j*, wood fibre; *k*, starch granule; *l*, fat; *m*, air-bubble.

become the left, or *vice versa*. A piece of tape twisted upon itself represents how this twisting is produced.

(*h*) *Woollen fibres* closely resemble hair, but as a rule are smaller and not so dark in color. The irregular surface markings representing the ensheathing cells is very distinct, but they have no granular centre.

(*i*) *Flax or linen* fibres resemble cotton, but do not twist upon themselves. They are striated longitudinally and crossed at short intervals by dark transparent lines, and are broken with an irregular fracture similar to a round pencil broken sharply. These fibres are usually round.

(*j*) *Silk fibres* are small and glistening, with fine irregular lon-

gitudinal markings and break nearly at a right angle similar to linen. Their glistening appearance, however, is the chief point of difference from linen.

All these fibres may be tinged blue by the indican of the urine, but this is especially noticeable in the cotton fibres.

(*k*) *Starch granules* are frequently found in the urine when starch powder has been dusted upon the genitals, as is frequently the case in young children. They are readily recognized by their elevated portion or hilum, and the surrounding dark and light-colored rings. The application of a little iodine will turn them blue.

(*l*) *Tea-leaves* also find their way into the urine and appear as irregular masses, having two or three light spots with a dark centre from which a spiral thread springs, looking like a partially uncoiled wire spring or the simple spiral may be all that will be found. There are, however, many other vegetable substances that have this spiral appearance.

(*m*) *Wood* and *vegetable.*—Small fragments of wood fibres and all kinds of vegetable substances occasionally find their way into the urine.

(*n*) *Finger markings* are not of infrequent occurrence upon the glass circles and are often thought to be indicative of some urinary change until they are recognized as foreign elements.

Out of the preceding list the substances which are most commonly found in connection with urinary analysis are air, oil, hair, cotton, wood, linen, and feathers. The substances most frequently mistaken for casts are hair, wool, cotton, linen, and dirt. Therefore, these are the foreign bodies which every examiner should become as familiar with as those of intrinsic origin.

CHAPTER XV.

ANIMAL ORGANISMS.

ECHINOCOCCUS; FILARIA SANGUINIS HOMINIS; BILHARZIA HÆMA-
TOBIA; TRACHINÆ CYSTICA; EUSTRONGYLUS SEU STRONGYLUS
GIGAS; TETRASTOMA RENALIS; SPURIOUS ENTOZOA; PEDICULUS
PUBIS.

There are only a few parasites which infest the human body and
make their escape by the urinary channel, and there are a few that
may get in the urina from the outside after it has been voided.

Ecchinococcus.—The scolices and hooklets of this parasite may oc-
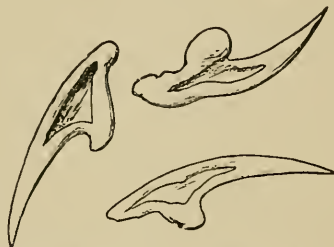
FIG. 93.—HOOKLETS FROM SCOLEX OF TÆNIA ECHINOCOCCUS. × 750.

(Delafield and Prudden, " Handbook of Pathological Anatomy and Histology.")

casionally find their way out of the body with the urine. Such cases
are recorded, and are probably due to the rupture of an hydatid cyst
in the kidney. When viewed under the microscope with a low power,
the scolices appear to be about the size of a millet seed, and are either
round or oval, and have at one end a dark colored zone or disk. The
body is small and granular, upon one extremity of which minute
suckers can be made out; with a higher power, their circle of hook-
lets can be seen, and the four suckers placed laterally and behind the
hooklets are now distinctly visible. Free hooklets are often found in
the urine at the same time.

(*b*) *Filaria sanguinis hominis, F. Bancrofti.*—In the embryonic

state, they are about $\frac{1}{150}$ of an inch (6 mm.) long, pointed at one end and blunt at the opposite. When fully developed, they are hair-like and from three to four inches (7 to 10 centimetres) in length. They vary in width from $\frac{1}{200}$ (8 mm.) to $\frac{1}{100}$ of an inch (4 mm.).

Their growth and development is quite peculiar. The parent worm lives in the lymphatics; the embryo escapes from the uterus of the mature worm, and finds its way along the lymphatic channels to the thoracic duct, and in this way ultimately reaches the blood-vessels. They originate more frequently in the lymphatics of the scrotum and leg, and appear in the blood most abundantly in the evening and up to midnight; after this hour, they gradually disappear until 8 or 9 o'clock A.M., when they are entirely absent from the blood for the remainder of that day.

FIG. 94.—SCOLICES OF TÆNIA ECHINOCOCCUS. × 60.

In one, the rostellum is projected, in the others it is withdrawn. (Delafield and Prudden, 'Handbook of Pathological Anatomy and Histology.")

"This phenomenal filarial periodicity is apparently an adapta-tion of the habits of the parasite to those of the female of a peculiar species of mosquito, which preys on the blood at night, and thus imbibes the young filaria, to which it acts as an intermediate host. Having entered the stomach of the mosquito, the filaria undergoes a metamorphosis, eventuating in its becoming possessed of an alimentary canal, rudimentary organs of generation, increased size, great activity, and a circumoval crown of papillæ. The latter is the boaring appa-ratus, which enables the animal to leave the body of the mosquito when this insect dies, after depositing her eggs on the water, and to traverse the human tissues to which it gains access, probably by being swallowed in drinking water." This history is probably more ingenious than real.

The filaria has been found in the blood, however, in cases of chyluria, nevoid elephantiasis, or lympho-sarcoma, varicose and indurated groin glands, galactocele, ascites with milky fluid, *craw-craw*, lymphatic fever, and certain kinds of lymphatic abscesses.

It has been found in the urine in connection with chyluria and nevoid elephantiasis. It may possibly find its way into the urine of
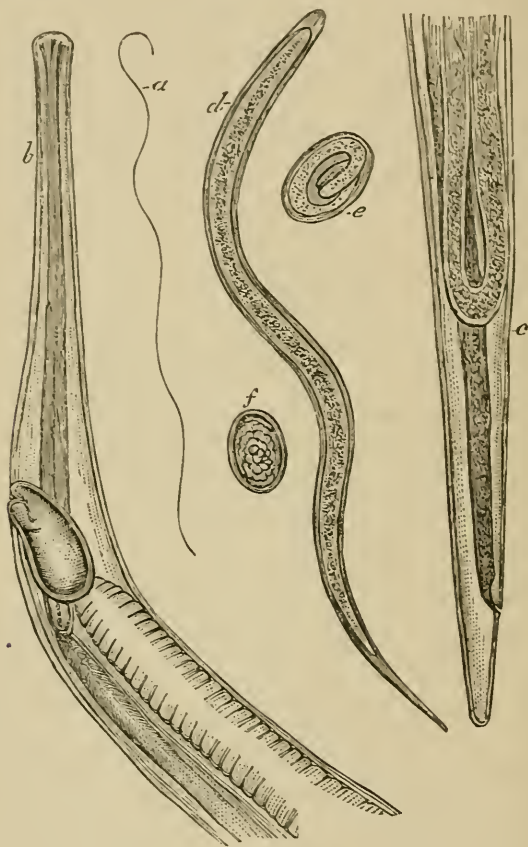
FIG. 95.—FILARIA SANGUINIS HOMINIS OR BANCROFTI.

a. Female (natural size); *b.* head and neck (× 55 diam.); *c.* tail; *d.* free embryo × 400 diam.; *e*, egg containing embryo; *f*, egg showing the yolk. After Cobbold. (London *Lancet*, October 6th, 1877, p. 495.)

the other enumerated diseases, but, up to the present time, has not been so recorded.

(*c*) *Bilharzia hæmatobia.*—This name was given to this parasite by Professor Cobbold in 1851, from the fact that Dr. Bilharz,

of Cairo, was the first to discover the entozoon. The worm was first found in the portal vein of a man, next in the corresponding vein of a monkey, and at first was supposed to be a *distoma*, but it is now generally known as the *Bilharzia hæmatobia*. Later on, it was found in the mesenteric and vesical veins, and also in other parts of the body, producing formidable diseases, and, finally, the parasitic hæmaturia.

Dr. John Harley next discovered that a form of epidemic hæmaturia at the Cape of Good Hope was due to a parasite which he considered a new species. Later researches, however, go to prove that it was the same Bilharzia described by Dr. Bilharz, and this conclusion is now pretty generally accepted. But the researches of Dr.
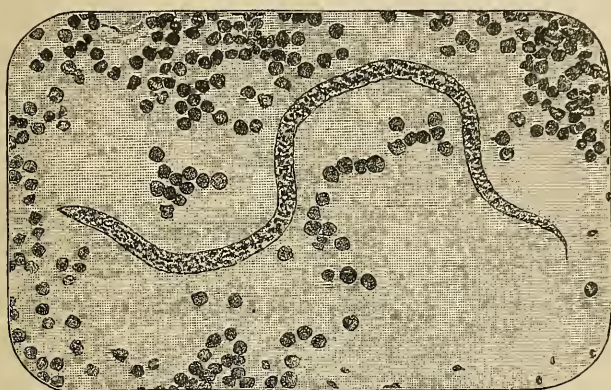
FIG. 96.—FILARIA IN HUMAN BLOOD.
After a photograph published by Dr. MacKenzie.

Harley showed a much wider geographical range for this parasite than had previously been supposed.

It differs from all the varieties of flukes in having separate sexes. The female is a very slender worm resembling filaria-form nematoids.

During copulation, the female is lodged in a long slit-like grove or gynæcophoric canal with which the male is furnished. The ova measure from $\frac{1}{180}$ to $\frac{1}{160}$ of an inch in length, and are sharply pointed at one end. They are a form of ciliated embryo, and an extended description will be found by Dr. Cobbold, *British Medical Journal*, 1872.

Both the mature worm and ova are found in the urine in this peculiar form of hæmaturia.

(*d*) *Trachinæ cystica* of Dr. Saulsbury.—In this case, the exact

species have not been fully determined, having been met with in only a few cases. By some it is thought to be identical with the filaria piscum; by others, the spiroptera hominis.
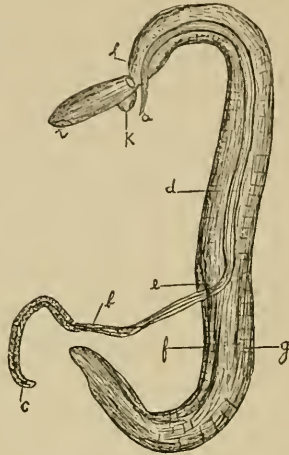
FIG. 97.—BILHARZIA HÆMOTOBIA. × about 15 times.

a, *b*, and *c*, the female, partly placed in the gynæcophorous canal of the male; *a*, anterior extremity; *c*, posterior extremity; *d*, body seen within the canal; *c*, *f*, *g*, *h*, and *i*, the male; *e*,*f*, gynæcophorous canal, from which the female has been partly extracted; *i*, buccal sucker; *k*, ventral sucker; between *i* and *k*, the trunk; after *k*, the tail. After Bilharz.

(*e*) *Eustrongylus* or *Strongylus gigas*.—This form of entozoa is more frequent in lower animals than in man. The worm is commonly
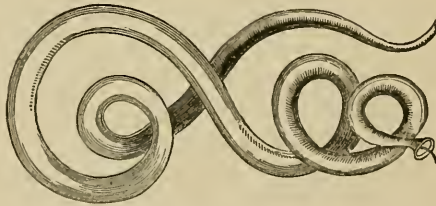
FIG. 98.—STRONGYLUS SEU EUSTRONGYLUS GIGAS.

found in the kidney or pelvis, and may possibly find its way down the ureter, and in this way make its escape from the body through the urethra.

Tetrastoma renalis.—This entozoon was found in the urine in one case by Lucarella, and described by Dellechiaji.

SPURIOUS ENTOZOOA.

There are a number of animal organisms which may find their way into the urine from the outside, such as the vorticella, the amœba, and various forms of the infusoria.

Under this heading may also be included the spiroptera hominis of Rudolphi, the disposoma crenata of Farre, and the dætylius aculeatus of Curling.

PEDICULUS PUBIS.

The pediculus pubis also finds its way into the urine, as illustrated

FIG. 99.—PEDICULUS PUBIS FOUND IN URINE. × 125.

by a drawing from one found in the urine.

CHAPTER XVI.

ANALYSIS OF THE CASE. INDICATIONS AS TO DIAGNOSIS AND TREATMENT.

ANALYSIS OF THE CASE.

A careful review of each sample examined, in conjunction with the clinical history, will usually make the diagnosis clear and positive. This is especially true in reference to the lesions so long grouped together under the common term Bright's disease. It is positively affirmed that, by a close observance of the laws already advanced in reference to the methods of production and the rules given for diagnosis, the existing lesions can in every instance be diagnosticated with great accuracy. It may be argued that such precision in diagnosis does not materially change the method of treatment; in which there is perhaps much truth, but it enables a more positive prognosis to be made and renders the treatment less empirical, and offers a far more certain prospect for recovery by a proper selection of remedial agents.

By reviewing closely the clinical history and the urinary findings, both at the bedside and at the necropsy, in over a hundred cases, an accurate diagnosis has resulted in every instance. A striking case in point is recalled where, by the application of these rules to the urinary analysis alone, an accurate diagnosis was made without seeing the patient until the necropsy, which fully confirmed the opinion previously expressed. This instance was an accidental injury in which no renal lesion was suspected, and was apparently developed as the result of the surgical accident, and caused the death of the patient.

This case is cited to show what accuracy in diagnosis can be attained, and how often an unobserved renal lesion may be a prominent factor in reference to prognosis.

To accomplish this accuracy in diagnosis, the examiner must make himself thoroughly familiar with the microscopic histological changes wrought in the kidneys and liver in connection with the different renal lesions. He must also be thoroughly familiar with the microscopic appearances of the urine, as it is by this careful microscopic examina-

tion, and a proper interpretation of what is found, that he is enabled to determine with positiveness the existing renal lesion.

A chemical examination alone yields comparatively little information in relation to the physiological phenomena of the body and their abnormal workings; but in conjunction with the microscopic results, a wonderful degree of precision is obtained, not only in connection with diseases of the kidneys, but in all diseases, and especially in connection with those originating in a faulty physiological function of the liver.

INDICATIONS AS TO DIAGNOSIS AND TREATMENT.

A thorough study of urinary analysis, and especially the microscopic part, will often make a diagnosis sure, which otherwise would remain obscure. This is true not alone in reference to renal lesions, but equally so in hepatic diseases.

Having obtained an accurate diagnosis, with a clear conception of the pathological processes and the interrupted or modified physiological phenomena, a critical study of the clinical symptoms will enable the examiner to prognosticate with a wonderful degree of accuracy.

Treatment based upon such knowledge enables the prescriber to anticipate pathological processes, to strengthen the enfeebled physiological functions, and in many instances enable or cause the system to completely repair the damage, thus effecting a cure where otherwise a fatal issue would be the result.

Treatment now becomes a fixed principle; a cause to be removed, and an abnormal and enfeebled system to be placed in a position to restore its damaged tissues and organs to their normal state. Having fully comprehended these principles, a specific virus, drug, or mineral water cannot be expected to cure these complex physiological and pathological problems. It must be clear to every one that this is impossible. The main object should be to discover where the physiological action is most at fault, and rectify it if possible. In this way each faulty action can be treated and removed in the order of its importance, and many permanent cures will be effected which otherwise would terminate in an early and untimely death.

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